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Associations between gestational diabetes mellitus and elevated HbA_{1c} early postpartum in a multi-ethnic population

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Abstract

Aims: To investigate the prevalence of elevated HbA_{1c} 14 weeks postpartum in different ethnic groups and in women with and without gestational diabetes mellitus (GDM) in the index pregnancy and to explore demographic and biological factors from early pregnancy associated with elevated HbA_{1c} (HbA_{1c} ≥5.7% (≥39 mmol/mol)) postpartum.

Methods: From a cohort study in Oslo, Norway, we included 570 pregnant women, examined in gestational week 15, 28, and 14 weeks postpartum. The association between elevated HbA_{1c} and demographic and biological factors were assessed by logistic regression analyses.

Results: The prevalence of elevated HbA_{1c} postpartum was 23% in the total population, 15% among Western Europeans and 28% among women with ethnic minority background ($p<0.01$). In ethnic minorities elevated HbA_{1c} was found in 39% of women with recent GDM diagnosed by the World Health Organization 2013 criteria and in 21% of women without GDM ($p<0.01$), compared to 22% and 13% in Western Europeans ($p=0.11$). We found independent associations between elevated HbA_{1c} and ethnic minority background (OR 2.0, 95% CI 1.27, 3.18), and GDM (OR 2.04, 95% CI 1.35, 3.10) ($p<0.01$).

Conclusions: The prevalence of elevated HbA_{1c} postpartum was 23%, and significantly higher among women with ethnic minority background irrespective of GDM.

Key words: HbA_{1c}, Gestational diabetes mellitus, ethnicity, postpartum.

1. Introduction

Haemoglobin A_{1c} (HbA_{1c}) is now used as the preferred diagnostic test for type 2 diabetes (T2DM) and values of 48 mmol/mol (6.5%) or above is diagnostic for diabetes after a repeated test [1]. There is still controversy defining a HbA_{1c} level that can be used to identify persons at risk for T2DM, however HbA_{1c} between 42 and 46 mmol/mol (6.0% and 6.4%) is associated with increased risk of developing T2DM [2]. There is a strong association between gestational diabetes mellitus (GDM) and development of T2DM [3, 4]. Women with GDM have impaired β-cell function in combination with insulin resistance, that contributes to increased risk of T2DM later in life [5]. Although most clinical guidelines recommend a standard oral glucose tolerance test (OGTT) to women with GDM 6-12 weeks postpartum [6, 7], the adherence is often poor. Several barriers have been identified such as time constraints, care of the new-born, breastfeeding and the burden of an OGTT [8].

Recently the UK National institute of Health and Care Excellence (NICE) and The American Diabetes Association (ADA) have proposed measuring HbA_{1c} as an alternative, more user friendly test, with HbA_{1c} ≥5.7% (≥39 mmol/mol) indicating high risk of T2DM in women with recent GDM [1, 9]. HbA_{1c} postpartum can be affected by iron deficiency and blood loss during delivery [10], indicating that HbA_{1c} can be unreliable early postpartum and that this test should not be performed earlier than 3-4 months after delivery [1]. Another alternative test might be fasting plasma glucose (FPG), with cut-off limit >6.0 mmol/L as suggested by NICE and 5.6 mmol/L by ADA and others [11] to identify women with high risk of having or developing T2DM [1]. Combining FPG ≥5.6 mmol/L and HbA_{1c} ≥5.7% (≥39 mmol/mol) will improve the identification of women with abnormal glucose tolerance [11].

Studies outside pregnancy indicate that persons with African-American and South Asian background have higher HbA_{1c} levels compared to Caucasian- Americans, especially if glucose intolerant [12-14], the reasons however remain largely unknown. We have so far not

identified any studies that have used the World Health organization (WHO) 2013 definition for GDM (GDM_{2013}) [15] postpartum to identify women at risk for T2DM.

In this study, our aims were to investigate the prevalence of HbA_{1c} ≥5.7% (≥39 mmol/mol) 14 weeks postpartum in different ethnic groups and in women with and without GDM_{2013} in the index pregnancy, and to explore demographic and biological factors from early pregnancy that are independently associated with HbA_{1c} ≥5.7% (≥39 mmol/mol) postpartum in a multi-ethnic population.

2. Methods

2.1. Study population and data collection

The methods of the STORK Groruddalen study have been described in detail elsewhere [16]. From May 2008 to May 2010, healthy pregnant women attending primary antenatal care at three public Child Health Clinics in Eastern Oslo, Norway, were asked to participate in this population-based cohort study [16]. Women with pre-pregnancy diabetes or other diseases necessitating intensive hospital follow-up during pregnancy were excluded. Overall, 823 (74% of eligible women) were included, 59% had ethnic minority background [16]. The participation rate was 64-82% in the different ethnic groups. Data from questionnaires and anthropometric measurements were collected by specially trained midwives according to protocol at mean gestational week 15.0 (SD 3.3) (visit 1), mean gestational week 28.3 (1.3) (visit 2) and 14.2 (2.7) weeks postpartum (visit 3) [16].

The study protocol was approved by the Regional Ethics Committee (2007/894) and the Norwegian Data inspectorate.

2.2.Variables

Maternal age at inclusion was self-reported. Parity was categorised as nulliparous or multiparous (≥1), referring to status before the current pregnancy. Ethnicity was defined by country of birth or that of the participant's mother if she was born outside Europe or North-America. Ethnic origin was further categorized as Western Europe, and ethnic minority women, consisting of South Asia, Middle East, Africa, East Asia and Eastern Europe [16]. Education was categorised as lower level (<12 years) or higher level (≥12 years). Family history of diabetes was self-reported and categorized as yes or no.

Height was measured to the nearest 0.1 cm using a fixed stadiometer at inclusion. Body weight was measured with a bioelectrical impedance analysis scale (Tanita-BC 418 MA, Tanita Corporation, Tokyo, Japan) [17], at visit 1 and visit 3, and body mass index (BMI) (kg/m^2) was calculated. Systolic blood pressure (mmHg) and diastolic blood pressure (mmHg) were measured with a validated electronic device Omron HEM-7000-E M6 Comfort (Omron HealthCare, Kyoto, Japan) [18, 19]. According to protocol, blood pressure was measured on the dominant arm in a sitting position, after at least 5 minutes rest [18]. At each visit, blood pressure was measured three times, in the morning hours. Mean values of the two last readings were used for analyses.

2.3. Biological parameters

At baseline, visit 2 and visit 3 venous blood was sampled in the morning after an overnight fast and sent for routine analyses at the Akershus University Hospital and Hormone Laboratory, Oslo University Hospital [16].

The main outcome variable HbA_{1c} was measured in venous EDTA blood with HPLC (Tosoh G8, Tosoh Corporation) [20], and categorised as elevated HbA_{1c} (HbA_{1c} ≥5.7% (≥39 mmol/mol)), and normal HbA_{1c} (HbA_{1c} <5.7% (<39 mmol/mol)). For HbA_{1c} the analytical coefficient of variation (CVa) was 1.0%. Haemoglobin (g/dL) was measured by Sysmex XE-5000, (Sysmex Corporation). Fasting total triglycerides (mmol/L) HDL-cholesterol (mmol/L) and LDL-cholesterol (mmol/L) were analysed in serum with a colorimetric method (Vitros 5.1 FS, Ortho clinical diagnostics). A standard 75 g OGTT was performed at visit 2 [16] and venous blood glucose was measured on site with a plasma calibrated HemoCue 201+ (Angelholm, Sweden). During the study women were diagnosed with GDM by the WHO 1999 criteria (WHO_{1999}) (FPG ≥7.0 or 2-h plasma glucose (PG) ≥7.8 mmol/L) [21]. Women with 2-h values 7.8-8.9 mmol/L were given lifestyle advice and referred to their general

practitioner for follow-up, and women with FPG ≥7.0 mmol/L or 2-h values ≥9.0 mmol/L were referred to specialist care [20]. GDM by the WHO_{2013} criteria (FPG ≥5.1 or 2-h glucose ≥8.5 mmol/L; no 1-h value available) [20] is also reported. We used the new diagnostic criteria for GDM by the WHO_{2013} [15] in this study. At visit 3 OGTT was only performed in the subset of women with previous GDM_{1999} who returned for follow-up visit (n=88 of 89).

2.4. Statistical analyses

Clinical and biochemical parameters by ethnicity are presented as mean (95% confidence interval (CI)) and proportions (%). Group differences of numerical variables were tested by independent t-tests and differences in proportions between groups were established using two-sample tests of proportions. The association between elevated HbA_{1c} postpartum and demographic and biological factors in the index pregnancy, including GDM_{2013} and other components of the metabolic syndrome (BMI, systolic blood pressure and diastolic blood pressure, triglycerides) were first estimated by univariate logistic regression analysis to identify factors associated with elevated HbA_{1c} postpartum (Table 2). We performed multiple logistic regression analyses. Model 1 was adjusted for ethnicity, age, parity, education and family history of diabetes. Model 2 was additionally adjusted for BMI, systolic blood pressure, GDM_{2013}, blood haemoglobin and serum triglyceride concentrations. In model 3 we used backward selection and only significant factors were retained. The associations between elevated HbA_{1c} and demographic and biological factors are presented as odds ratios (OR) with 95% CI. We tested for and found no interactions in the logistic regression analysis. A sensitivity analysis was performed to explore the effect of excluding women with post-delivery anaemia (haemoglobin concentration <12 g/dL) and women who attended visit 3 before 13 weeks postpartum [22]. P-values <0.05 were regarded as statistically significant.

SPSS (IBM SPSS Statistic, version 21: IBM, Armonk, NY, USA) and Stata/SE 13.1 were used for all analyses.

2.5. Sample selection and study procedures

Of the 823 women included at visit 1, [16] women from Central and South America (n=12) were excluded due to low numbers. Of the remaining 811 eligible women, 762 met at visit 2 and 655 met at visit 3. The study sample consists of 570 women with valid data on HbA_{1c} from the postpartum visit. Among the 811 eligible women, there were no differences between the study sample and women without valid HbA_{1c} postpartum with respect to age (p=0.15), BMI (p=0.58) and parity (p=0.44). However, the study sample consisted of a larger proportion of women with ethnic minority background (p<0.01), which can be explained by a prioritization of blood sampling from ethnic minority women and women with GDM_{1999} diagnosed at visit 2.

3. Results

3.1. Prevalence of elevated $HbA1_c$ postpartum

Characteristics of women with elevated and normal HbA_{1c} at 14 weeks postpartum in Western Europeans and ethnic minorities are shown in table 1, and for all the six ethnic groups in the supplementary tables S1 and S2.

In total, 23% of the participants had elevated HbA_{1c} postpartum, 15% among Western Europeans and 28% in ethnic minority groups ($p<0.01$) (Table 1). Figure 1 presents the prevalence of elevated HbA_{1c} for six ethnic groups. A higher proportion of women diagnosed with GDM_{2013} were identified among those with elevated HbA_{1c} postpartum, although the findings were significant only in the ethnic minority group ($p< 0.01$) (Table 1). Figure 2 shows the prevalence of elevated HbA_{1c}, stratified by ethnicity and GDM status by WHO_{2013} criteria in the index pregnancy. The overall prevalence of elevated HbA_{1c} was 34% among women with previous GDM compared with 18% among women without GDM ($p<0.01$) (Figure 2). The corresponding prevalence were higher among ethnic minority women (39% and 21%, $p<0.01$) compared to Western women (22% and 13%, $p=0.11$). Among women with elevated HbA_{1c}, the proportion of women with GDM_{2013} in the index pregnancy was larger than among women with normal HbA_{1c} (Table 1 and S1).

3.2. Demographic and biological factors

Ethnic minorities with elevated HbA_{1c} postpartum were older ($p<0.01$), had lower haemoglobin ($p=0.02$), higher levels of triglycerides ($p=0.03$) and higher blood pressure ($p<0.05$) compared to those with normal HbA_{1c}. In Western Europeans similar trends were observed, without reaching statistical significance, probably due to lower numbers and thereby lack of statistical power. However, the mean haemoglobin level was lower in women with elevated HbA_{1c} compared to women with normal HbA_{1c}, irrespective of ethnic

background (Table 1). Within the Western European and ethnic minority group there were significant differences in mean HbA_{1c} levels for women diagnosed with GDM_{2013}, 37 mmol/mol (5.5%) versus women not diagnosed with GDM, 36 mmol/mol (5.4%) ($p<0.01$). Of the 89 women diagnosed with GDM_{1999} at visit 2 (Table S1 and S2), 88 returned for OGTT postpartum, nine women (10%) had a 2-h-PG ≥7.8 mmol/L of whom five had elevated HbA_{1c}. The prevalence of women with FPG ≥5.6 mmol/L postpartum was 3.3% (n=7), among Western Europeans and 7.1% (n=25) among ethnic minorities.

3.3. Elevated HbA_{1c} postpartum is associated with ethnicity and GDM_{2013}

Ethnicity, age, levels of haemoglobin and triglycerides and a GDM_{2013} diagnosis were associated with elevated HbA_{1c} in univariate logistic regression analyses (Table 2). After adjustments for a range of demographic and biological factors we found independent associations between elevated HbA_{1c} postpartum and ethnicity (OR 2.0, 95% CI 1.27, 3.18) and between elevated HbA_{1c} and GDM_{2013} (OR 2.04, 95% CI 1.35, 3.10). Age and triglycerides were also significantly associated with elevated HbA_{1c} (Table 2).

In sensitivity analyses excluding women with anaemia (haemoglobin concentration <12 g/dL) and women who had met before 13 weeks postpartum (9.1%, n=52), the associations observed between elevated HbA_{1c} postpartum and ethnicity, age, triglycerides and GDM_{2013} were substantially unchanged (data not shown).

4. Discussion

In this cohort of pregnant women, 23% had elevated HbA_{1c}, defined as ≥5.7% (≥39 mmol/mol) four months postpartum. However, the prevalence differed strongly by ethnic group and GDM status in the index pregnancy. Twenty-two percent of Western European women and 39% of ethnic minority women with previous GDM by the WHO_{2013} criteria had elevated $HbA_{1c,}$ as defined by NICE and ADA. However, even among women without GDM in the index pregnancy, 13% of Western and 21% of ethnic minority women had elevated $HbA_{1c.}$ GDM in the index pregnancy and ethnic minority background provide separately a doubling of risk of elevated $HbA_{1c.}$ The mean haemoglobin levels were lower in women with elevated $HbA_{1c,}$ but adjusted for other factors, haemoglobin was no longer independently associated with elevated $HbA_{1c.}$

4.1. Strengths and limitations

The strengths of this study are the multi-ethnic, population-based cohort design, universal use of OGTT in gestation week 28, the broad data set and the high participation rates across the ethnic groups, as the study methods were adapted to reach groups often excluded in research. We consider the population to be fairly representative for the main ethnic groups of pregnant women in Oslo. The loss to follow-up at gestational week 28 was minor [16]. However, our findings may be affected by methodologic limitations due to heterogeneity within the ethnic minority group and the small numbers of participations in some groups. A major shortcoming of our study is that we lack OGTT-data for a majority of the women at the postpartum visit hence we cannot directly compare OGTT-results with the HbA_{1c} measurements. Only women who were diagnosed with GDM by the WHO 1999 criteria, were offered OGTT postpartum, and of these 10% had impaired glucose tolerance. We also lack data on HbA_{1c} postpartum for 13% of the women, due to logistic reasons.

4.2. Comparison with other studies

In our study 34% of women with GDM in the index pregnancy had elevated HbA_{1c} as early as 14 weeks postpartum and these women are therefore at risk of developing T2DM, in line with results from a previous study [23]. The prevalence of T2DM is increasing worldwide, and related to a complex combination of modifiable risk factors such as overweight, physical inactivity, previously identified elevated glucose level, abnormal lipids, hypertension, and non-modifiable risk factors such as age, ethnicity and genetics [24]. A higher proportion of ethnic minority women had elevated $HbA_{1c,}$ in accordance with previous studies reporting higher HbA_{1c} levels among ethnic minorities [12, 13]. In the present study we observed that ethnic minority women with elevated HbA_{1c} had higher levels of triglycerides compared to those with normal HbA_{1c}. Elevated triglycerides is an important component of the metabolic syndrome associated with central adiposity [25] and the finding may signal that metabolic syndrome is an important determinant of elevated HbA_{1c} postpartum. We adjusted for a range of demographic and biological factors that could affect the association between GDM_{2013} and elevated HbA_{1c} postpartum and found that already 14 weeks postpartum women with GDM in the index pregnancy have a twofold risk of elevated HbA_{1c} compared with women without GDM.

HbA_{1c} ≥5.7% (≥39 mmol/mol) postpartum is proposed as a cut-off to identify women with previous GDM at risk of T2DM [1]. An HbA_{1c} test may be more feasible than OGTT as HbA_{1c} now is the preferred diagnostic test for diabetes and since adherence to recommendations to use OGTTs postpartum is poor. The concentration of HbA_{1c} depends on glycaemia and the lifespan of the erythrocytes [26]. Lower levels of HbA_{1c} in healthy pregnant women compared to non-pregnant women [27] could be explained by an increase in red blood cell turnover [26]. Caucasians seem to have lower HbA_{1c} compared to other ethnic groups with the same plasma glucose level e. g African-Americans and Asian Americans [12,

13]. In a previous study from India, a high prevalence of HbA_{1c} ≥5.7% (≥39 mmol/mol) among young Indians was observed [14]. This was partially explained by high prevalence of iron deficiency anaemia that prolongs erythrocyte survival and disproportionally increase HbA_{1c} levels [14]. In our study, we observed small, but significant and consistent differences in haemoglobin levels between groups with HbA_{1c} below or above the ≥5.7% (≥39 mmol/mol). Women with elevated HbA_{1c} had lower haemoglobin level, as the study from India and a previous study from South Korea [28]. Major causes of postpartum anaemia are iron deficiency during pregnancy, in combination with bleeding anaemia due to blood loss at delivery [22], that may influence HbA_{1c} values. Although the majority of our participants met after 13 weeks postpartum we cannot exclude that increased turnover of red blood cells during pregnancy might have affected our results.

To prevent development of T2DM in women with previous GDM, information about risk factors and lifestyle advice is essential. A Finnish study found that women at high risk of T2DM, both with and without previous GDM, benefitted from lifestyle interventions consisting of group based information and exercise, based on the principles of empowerment in a primary healthcare setting [29]. However, in this study [29] few women were motivated to participate indicating that there is a need for innovative lifestyle interventions. Women with known risk factors for T2DM, such as overweight, obesity and elevated HbA_{1c} [1, 9, 24], may benefit from targeted prevention programs. In a previous study of women with a history of GDM, both lifestyle intervention and treatment with metformin were effective in preventing or delaying development of T2DM [23].

To conclude, we found a high prevalence of women with elevated HbA_{1c} postpartum, suggesting that a substantial proportion of women have high risk of future T2DM, irrespective of previous history of GDM_{2013}. The general practitioner should therefore have awareness on women with elevated of HbA_{1c} levels to prevent development of T2DM. Several demographic

and biological factors were associated with elevated HbA_{1c}, suggesting that more research is needed before general recommendations to replace the postpartum OGTT with the use of HbA_{1c} ≥5.7% (≥39 mmol/mol) to identify women at high risk for T2DM are implemented.

Disclosure

The authors have approved the final article.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Tables

Table 1. Demographic and biological factors stratified by ethnicity and HbA_{1c} ≥5.7% (≥39 mmol/mol) (n=131) and <5.7% (<39 mmol/mol) 14 weeks postpartum. Values are mean (95% CI) or numbers (%).

	Western Europe, n=215					**Ethnic minorities, n=355**					
	≥5.7% (≥39 mmol/mol) n=33 (15%)		**<5.7% (<39 mmol/mol)** n=182 (85%)		**P-value***	**≥5.7% (≥39 mmol/mol)** n=98 (28%)		**<5.7% (<39 mmol/mol)** n=257 (72%)		**P-value***	**P-value****
	Mean	95% CI	Mean	95% CI		Mean	95% CI	Mean	95% CI		
HbA_{1c} [b] (mmol/mol)	**40**	**(40, 40)**	**36**	**(34, 36)**	**<0.01**	**40**	**(40, 41)**	**34**	**(34, 34)**	**<0.01**	0.10
HbA_{1c} [b] (%)	**5.8**	**(5.8, 5.8)**	**5.4**	**(5.3, 5.4)**	**<0.01**	**5.8**	**(5.8, 5.9)**	**5.3**	**(5.3, 5.3)**	**<0.01**	0.10
Age (years)	31.6	(29.2, 33.3)	30.7	(30.0, 31.5)	0.30	**30.2**	**(29.2, 31.3)**	**28.5**	**(28.0, 29.1)**	**<0.01**	0.18
Nulliparous (%)	14 (42.4)		99 (54.4)		0.21	39 (39.8)		108 (42.0)		0.70	0.79
Haemoglobin (g/dL)	**12.4**	**(12.1, 12.7)**	**12.9**	**(12.7, 13.0)**	**0.01**	**12.2**	**(12.0, 12.4)**	**12.5**	**(12.4, 12.6)**	**0.02**	0.40
Body mass index (kg/m^2)	26.8	(24.4, 29.2)	25.7	25.0, 26.4)	0.36	26.7	(25.7, 27.7)	26.0	825.4, 26.6)	0.24	0.89
FPG[c] (mmol/L)	**4.9**	**(4.7, 5.1)**	**4.7**	**(4.7, 4.8)**	**0.02**	**5.0**	**(4.9, 5.1)**	**4.8**	**(4.7, 4.8)**	**<0.01**	0.25
Triglycerides (mmol/L)	1.0	(0.8, 1.2)	0.9	(0.9, 1.0)	0.47	**1.1**	**(1.0, 1.3)**	**1.0**	**(0.9, 1.1)**	**0.03**	0.16
HDL-cholesterol (mmol/L)	1.6	(1.4, 1.8)	1.6	(1.6, 1.7)	0.84	1.4	(1.4, 1.5)	1.5	(1.5, 1.6)	0.08	0.09
LDL-cholesterol (mmol/L)	3.1	(2.8, 3.4)	3.1	(3.0, 3.3)	0.89	3.2	(3.0, 3.3)	3.0	(2.9, 3.1)	0.10	0.74
Systolic blood pressure (mmHg)	106.6	(103.2, 110, 1)	105.7	(104.1, 107.3)	0.67	**104.9**	**(102.9, 107.0)**	**102.4**	**(101.0, 103.7)**	**0.04**	0.42
Diastolic blood pressure	71.8	(69.5, 74.0)	72.2	(71.0, 73.5)	0.76	**72.4**	**(70.7, 74.2)**	**69.8**	**(68.7, 70.9)**	**0.01**	0.67
(mmHg) GDM[a] (WHO_{1999}) (%)	5 (15.2)		26 (14.5)		0.93	**24 (25.5)**		**34 (13.7)**		**<0.01**	0.22
GDM[a] (WHO_{2013}) (%)	13 (39.4)		46 (25.7)		0.11	**49 (51.6)**		**77 (30.3)**		**<0.01**	0.23
Education level (<12	**17 (51.5)**		**55 (30.6)**		**0.02**	68 (69.4)		183 (71.8)		0.66	0.06
years) Family history of	9 (27.3)		35 (19.2)		0.29	46 (46.9)		110 (42.8)		0.48	0.05
diabetes											

[a]GDM: Gestational diabetes mellitus diagnosed at mean gestational week 28. [b]HbA_{1c}: Glycated Haemoglobin. [c]FPG: Fasting plasma glucose. Comparison of means is tested by independent t-test. Comparison of proportions is tested by chi-square test. *P-values for differences between groups with HbA_{1c} ≥5.7% (≥39 mmol/mol) and <5.7% (<39 mmol/mol). **P-values for comparison between Western Europeans versus Ethnic minorities: HbA_{1c} ≥5.7% (≥39 mmol/mol). Bold numbers indicate p-values <0.05.

Table 2. Logistic regression analysis of the association between HbA1c ≥5.7% (≥39 mmol/mol) 14 weeks postpartum and demographic and biological factors.

	Univariate			**Model 1** n=566, R^2=0.04			**Model 2** n=546, R^2=0.07			**Model 3** n=560, R^2=0.06		
	OR	(95% CI)	P-value*	OR	(95% CI)	P-value*	OR	(95% CI)	P-value*	OR	(95% CI)	P-value*
Ethnicity												
Western European	Reference			Reference			Reference					
Ethnic minority	**2.10**	**(1.36, 3.26)**	**<0.01**	**2.15**	**(1.32, 3.51)**	**<0.01**	**1.98**	**(1.17, 3.33)**	**0.01**	**2.00**	**(1.26, 3.18)**	**<0.01**
Age (years)	**1.05**	**(1.01, 1.10)**	**0.02**	**1.07**	**(1.02, 1.12)**	**<0.01**	**1.05**	**(1.00, 1.11)**	**0.03**	**1.05**	**(1.00, 1.09)**	**0.04**
Parity												
Multiparous, (≥1) Nulliparous	Reference			Reference			Reference					
	0.76	(0.51, 1.13)	0.18	1.08	(0.69, 1.69)	0.73	1.11	(0.70, 1.77)	0.66			
Education level (years)												
≥10	Reference			Reference			Reference					
<10	1.62	(0.99, 2.64)	0.05	1.28	(0.76, 2.17)	1.260.35	1.19	(0.68, 2.09)	0.53			
Family history of diabetes	1.47	(0.98, 2.19)	0.06	(0.83, 1.91)		0.29	1.12	(0.72, 1.73)	0.62			
Body mass index (kg/m^2)	1.03	(0.99, 1.07)	0.15				0.99	(0.95, 1.04)	0.76			
Haemoglobin (g/dL)	**0.79**	**(0.65, 0.97)**	**0.03**				0.82	(0.65, 1.03)	0.08			
Triglycerides (mmol/L)	**1.75**	**(1.25, 2.44)**	**<0.01**				1.41	(0.98, 2.05)	0.07	**1.49**	**(1.05, 2.12)**	**0.03**
Systolic blood pressure (mmHg)	1.01	(0.99, 1.03)	0.42				1.02	(0.99, 1.04)	0.15			
GDM_{2013} (reference: no GDM)	**2.37**	**(1.58, 3.55)**	**<0.01**				**2.07**	**(1.34, 3.21)**	**<0.01**	**2.04**	**(1.34, 3.10)**	**<0.01**

Demographic and biological factors are measured at mean gestational week 15. GDM_{2013} is measured mean gestational week 28. Model 1 is adjusted for ethnicity, age, parity, education and family history of diabetes. Model 2 is additionally adjusted for body mass index, haemoglobin, triglycerides, systolic blood pressure and GDM_{2013}. Model 3 includes only factors significantly associated with elevated HbA_{1c}. *Bold numbers indicate p-values <0.05.

Table S1. Characteristics of the cohort with HbA_{1c} ≥5.7% (≥39 mmol/mol) by ethnic groups, values are mean (SD) or numbers (%).

	Total	Western Europe		South Asia		Middle East		Africa		East Asia		Eastern Europe	
	n=131	n=33 (25)		n=47 (36)		n=16 (12)		n=14 (11)		n=11 (8)		n=10 (8)	
Visit 1 (gestational week 15)													
Age (years)	131	33	31.6 (4.8)	47	29.4 (5.1)	16	30.9 (5.3)	14	29.2 (5.9)	11	34.3 (3.7)	10	29.8 (4.0)
Nulliparous, n (%)	53	14	(42.4)	22	(46.8)	3	(18.8)	5	(35.7)	2	(18.2)	7	(70.0)
Education level (<12 years)	85	17	(51.5)	34	(72.3)	13	(81.3)	11	(78.6)	6	(54.5)	4	(40.0)
Body mass index (kg/m^2)	131	33	26.2 (6.1)	47	24.7 (4.7)	16	28.4 (5.6)	14	27.2 (4.6)	11	24.4 (4.2)	10	25.8 (5.1)
Triglycerides (mmol/L)	131	33	1.3 (0.7)	47	1.5 (0.5)	16	1.5 (0.7)	14	1.3 (0.6)	11	1.9 (0.9)	10	1.6 (1.1)
HDL-cholesterol (mmol/L)	131	33	1.7 (0.4)	47	1.7 (0.4)	16	1.6 (0.4)	14	1.9 (0.4)	11	2.0 (0.4)	10	1.7 (0.3)
LDL-cholesterol (mmol/L)	128	32	2.8 (0.7)	47	3.0 (0.7)	16	2.6 (0.8)	14	3.0 (1.0)	10	2.5 (0.7)	9	2.7 (0.4)
Systolic blood pressure (mmHg)	131	33	107.4 (9.3)	47	100.2 (9.7)	16	104.3 (10.1)	14	99.6 (11.8)	11	99.5 (10.1)	10	103.2 (11.7)
Diastolic blood pressure (mmHg)	131	33	69.2 (8.3)	47	66.2 (7.1)	16	67.7 (7.4)	14	63.0 (10.7)	11	65.6 (8.0)	10	68.0 (7.1)
HbA_{1c} [a] (mmol/mol)	130	32	36 (1.3)	47	37 (2)	16	37 (2)	14	36 (1.3)	11	37 (1.4)	10	36 (2)
HbA_{1c} [a] (%)			5.4 (0.2)		5.5 (0.3)		5.5 (0.3)		5.4 (0.2)		5.5 (0.2)		5.4 (0.3)
Haemoglobin (g/dL)	130	32	12.2 (0.8)	47	11.5 (1.1)	16	11.7 (1.0)	14	12.0 (0.9)	11	12.1 (0.8)	10	12.0 (0.9)
Fasting plasma glucose (mmol/L)	129	33	4.5 (0.4)	47	4.5 (0.4)	16	4.6 (0.6)	12	4.5 (0.4)	11	4.5 (0.3)	10	4.6 (0.8)
Visit 2 (gestational week 28)													
GDM[b] (WHO_{1999}), n (%)	29	5	(15.2)	13	(28.3)	4	(26.7)	1	(7.7)	3	(30.0)	3	(30.0)
GDM[c] (WHO_{2013}), n (%)	62	13	(39.4)	25	(53.2)	9	(60.0)	7	(53.8)	5	(50.0)	3	(30.0)
Family history of diabetes	55	9	(27.3)	28	(59.6)	7	(43.8)	4	(28.6)	3	(27.3)	4	(40.0)
Visit 3 (three months postpartum)													
2-h plasma glucose (mmol/L)	30	7	6.3 (1.3)	12	6.4 (1.4)	3	7.3 (1.1)	2	5.9 (0.6)	4	6.3 (2.0)	2	6.8 (0.7)

[a]HbA_{1c}: Glycated Haemoglobin. [b]GDM: Gestational diabetes mellitus. WHO_{1999} (FPG ≥7.0 mmol/L or 2-h PG ≥7.8 mmol/L. [c]GDM: WHO_{2013} (FPG ≥5.1 mmol/L or 2-h PG ≥8.5 mmol/L).

Table S2. Characteristics of the cohort with HbA_{1c} <5.7% (<39 mmol/mol) by ethnic groups, values are mean (SD) or numbers (%).

	Total n=439	Western Europe n=182 (42)		South Asia n=111 (25)		Middle East n=76 (17)		Africa n=25 (6)		East Asia n=22 (5)		Eastern Europe n=23 (5)	
Visit 1 (gestational week 15)													
Age (years)	439	182	30.7 (4.6)	111	28.1 (4.0)	76	29.3 (5.6)	25	28.5 (4.7)	22	29.2 (3.8)	23	27.5 (4.2)
Nulliparous, n (%)	207	99	(54.4)	44	(39.6)	25	(32.9)	13	(52.0)	11	(50.0)	15	(65.2)
Education level (<12 years)	238	55	(30.6)	73	(65.8)	62	(82.7)	22	(88.0)	15	(68.2)	11	(50.0)
Body mass index (kg/m^2)	439	182	25.6 (4.7)	111	24.2 (3.8)	76	26.3 (5.1)	25	27.1 (6.7)	22	22.1 (2.7)	23	23.5 (3.6)
Triglycerides (mmol/L)	438	182	1.2 (0.5)	111	1.4 (0.6)	76	1.3 (0.4)	24	1.1 (0.4)	22	1.6 (0.5)	23	1.1 (0.3)
HDL-cholesterol (mmol/L)	438	182	1.7 (0.4)	111	1.7 (0.4)	76	1.7 (0.4)	24	1.8 (0.5)	22	1.8 (0.5)	23	1.8 (0.3)
LDL-cholesterol (mmol/L)	438	182	2.7 (0.8)	111	2.8 (0.8)	76	2.8 (1.0)	24	2.9 (0.8)	22	2.4 (0.8)	23	2.8 (0.5)
Systolic blood pressure (mmHg)	436	182	105.0 (9.9)	109	97.6 (8.3)	76	99.7 (8.8)	24	101.7 (10.7)	22	97.7 (10.1)	23	107.5 (9.6)
Diastolic blood pressure (mmHg)	436	182	68.7 (8.0)	109	65.2 (7.3)	76	65.4 (8.1)	24	66.7 (6.8)	22	66.6 (6.7)	23	69.1 (6.5)
HbA_{1c} [a] (mmol/mol)	432	178	32 (1.3)	110	33 (1.9)	75	31 (1.9)	24	32 (1.9)	22	32 (2.5)	23	31 (1.9)
HbA_{1c} [a] (%)			5.1 (0.2)		5.2 (0.3)		5.0 (0.3)		5.1 (0.3)		5.1 (0.4)		5.0 (0.3)
Haemoglobin (g/dL)	431	178	12.3 (0.9)	110	11.8 (1.0)	75	12.0 (1.0)	23	11.6 (1.1)	22	11.9 (1.0)	23	12.4 (0.7)
Fasting plasma glucose (mmol/L)	431	181	4.4 (0.4)	108	4.5 (0.5)	75	4.5 (0.5)	22	4.3 (0.6)	22	4.3 (0.3)	23	4.4 (0.3)
Visit 2 (gestational week 28)													
GDM[b] (WHO_{1999}), n (%)	60	26	(14.5)	13	(12.1)	13	(18.1)	3	(12.0)	3	(13.6)	2	(8.7)
GDM[c] (WHO_{2013}), n (%)	123	46	(25.7)	43	(39.4)	22	(29.3)	3	(12.0)	4	(18.2)	3	(12.0)
Family history of diabetes	145	35	(19.2)	63	(56.8)	29	(38.2)	8	(32.0)	5	(22.7)	5	(21.7)
Visit 3 (three months postpartum)													
2-h plasma glucose (mmol/L)	58	23	5.8 (1.1)	16	5.8 (1.6)	14	5.9 (1.5)	1	-	3	5.6 (0.2)	1	-

[a]HbA_{1c}: Glycated Haemoglobin. [b]GDM: Gestational diabetes mellitus. WHO_{1999} (FPG ≥7.0 mmol/L or 2-h PG ≥7.8 mmol/L. [c]GDM: WHO_{2013} (FPG ≥5.1 mmol/L or 2-h PG ≥8.5 mmol/L).

Figure Legends

Figure 1. Prevalence of HbA_{1c} ≥5.7% (≥39 mmol/mol) with 95% confidence interval by six ethnic groups 14 weeks postpartum (n=131). Participants were from Africa (n=14), East Asia (n=11), Eastern Europe (n=10), South Asia (n=47), Middle East (n=16), Western Europe (n=33).

Figure 2. Prevalence of HbA_{1c} ≥5.7% (≥39 mmol/mol) with 95% confidence interval for the total population and by ethnic groups stratified by GDM.

Figure

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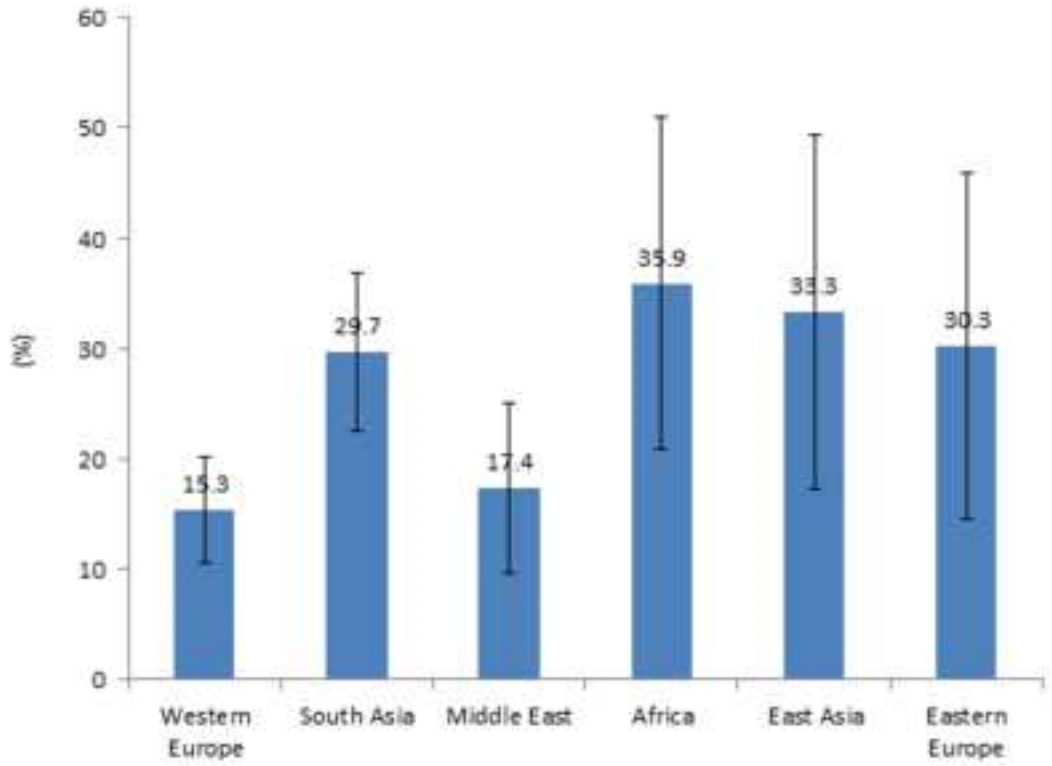

Figure

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