Maternal racial origin and adverse pregnancy outcome: a cohort study

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KEYWORDS: Cesarean section; gestational diabetes; large-for-gestational age; miscarriage; pre-eclampsia; preterm delivery; race; small-for-gestational age; stillbirth

ABSTRACT

Objective To examine the association between maternal racial origin and a wide range of adverse pregnancy outcomes after adjustment for confounding factors in obstetric history and maternal characteristics.

Methods This was a retrospective study in women with singleton pregnancies attending their first routine hospital visit at 11 + 0 to 13 + 6 weeks of gestation. Data on maternal characteristics, and medical and obstetric history were collected and pregnancy outcomes ascertained. Regression analysis was performed to examine the association between racial origin and adverse pregnancy outcomes including pre-eclampsia (PE), gestational hypertension (GH), gestational diabetes mellitus (GDM), preterm delivery (PTD), small-for-gestational age (SGA), large-for-gestational age (LGA), miscarriage, stillbirth and elective and emergency Cesarean section (CS).

Results The study population included 76,158 singleton pregnancies with a live fetus at 11 + 0 to 13 + 6 weeks. In addition to maternal characteristics and obstetric history, Afro-Caribbean racial origin was associated with increased risk for miscarriage, stillbirth, PE, GH, spontaneous PTD, GDM, SGA and CS. In women of South Asian racial origin there was increased risk for PE, GDM, SGA and CS, and East Asian race contributed to the prediction of GDM and SGA.

Conclusion Maternal racial origin should be combined with other maternal characteristics and obstetric history when calculating an individualized adjusted risk for adverse pregnancy outcome. Copyright © 2012 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

In developed countries women from minority racial groups have a higher prevalence of a wide range of adverse pregnancy outcomes, including miscarriage1,2, stillbirth3–5, pre-eclampsia (PE)6–13, gestational hypertension (GH)10, gestational diabetes mellitus (GDM)10,14–21, preterm delivery (PTD)10,22–26, delivery of small-for-gestational age (SGA)23,25,27–29 or large-for-gestational age (LGA)30,31 neonates and elective or emergency Cesarean section (CS)10,32,33. However, the studies reporting on the relationship between maternal racial origin and adverse outcomes have often not corrected for potential confounding variables, including maternal characteristics and medical or obstetric history.

The aim of this screening study was to examine the association between maternal racial origin and a wide range of adverse pregnancy outcomes after adjustment for confounding factors in obstetric history and maternal characteristics.

METHODS

This was a retrospective study in women attending their first routine hospital visit at three UK hospitals: King’s College Hospital, London; University College London Hospitals, London; and Medway Maritime Hospital, Kent. This visit, which was held at 11 + 0 to 13 + 6 weeks of gestation, included recording of maternal demographic characteristics and obstetric and medical history, measurement of maternal weight and height, ultrasound examination for the measurement of the fetal crown–rump length (CRL) and to determine gestational
In women with normal random blood glucose, administration of 75 g of glucose, was 7.8 mmol/L or carried out within 2 weeks. A diagnosis of GDM was made according to the guidelines of the International Society for the Study of Hypertension in Pregnancy. In all women random plasma glucose was measured at 24–28 weeks of gestation and, if the concentration exceeded the 95th percentile for gestation, respectively. In the investigation of the relationship between racial origin and GDM, we excluded pregnancies ending in miscarriage or stillbirth and those with spontaneous delivery before 34 weeks. The commonest causes of iatrogenic PTD in our cohort were PE and fetal growth restriction. In the investigation of the relationship between racial origin and iatrogenic PTD, we excluded pregnancies ending in miscarriage or stillbirth and those with spontaneous delivery before 34 weeks.

Data on pregnancy outcomes were collected from the hospital maternity records and from the women’s general medical practitioners. Participants completed a questionnaire on their age, racial origin (Caucasian, Afro-Caribbean, South Asian, East Asian or mixed), method of conception (spontaneous or assisted), cigarette smoking during pregnancy, history of chronic hypertension, history of Type 1 or Type 2 diabetes mellitus and obstetric history, including the outcome of each previous pregnancy. The questionnaire was then reviewed by a doctor together with the woman.

Outcome measures included miscarriage or stillbirth, PE or GH, GDM, spontaneous and iatrogenic PTD before 34 weeks, delivery of an SGA or an LGA neonate and delivery by elective or emergency CS. We excluded pregnancies with fetal aneuploidies or major defects diagnosed either prenatally or in the neonatal period, and pregnancies ending in termination for psychosocial reasons.

Miscarriage included spontaneous miscarriage and fetal death before 24 weeks’ gestation. Stillbirths were fetal deaths at or after 24 weeks. The diagnosis of PE and GH was made according to the guidelines of the International Society for the Study of Hypertension in Pregnancy. In GH the systolic blood pressure should be 140 mmHg or more and/or the diastolic blood pressure should be 90 mmHg or more on at least two occasions, 4 h apart, developing after 20 weeks of gestation in previously normotensive women in the absence of significant proteinuria. In PE there should be GH with proteinuria of 300 mg or more in 24 h, or two readings of at least ++ on dipstick analysis of midstream or catheter urine specimens if no 24-h urine collection is available. We also subdivided PE, according to gestational age at delivery, into early PE (<34 weeks) and late PE (≥34 weeks). In the investigation of the relationship between racial origin and PE or GH we excluded pregnancies ending in miscarriage or fetal death before 24 weeks.

Screening for GDM was based on a two-step approach. In all women random plasma glucose was measured at 24–28 weeks of gestation and, if the concentration was > 6.7 mmol/L, an oral glucose tolerance test was carried out within 2 weeks. A diagnosis of GDM was made if the fasting plasma glucose level was at least 6 mmol/L or the plasma glucose level, 2 h after the oral administration of 75 g of glucose, was 7.8 mmol/L or more. In women with normal random blood glucose, an oral glucose tolerance test was performed if they had persistent glucosuria, developed polyhydramnios or if the fetus became macrosomic. In the investigation of the relationship between racial origin and GDM we excluded pregnancies with prepregnancy diabetes mellitus Type 1 or Type 2 and those ending in miscarriage or delivery before 30 weeks because they might not have had screening and diagnosis of GDM.

Spontaneous PTD included those with spontaneous onset of labor and those with preterm labor rupture of membranes occurring before 34 completed weeks (238 days). In the investigation of the relationship between racial origin and spontaneous PTD, we excluded pregnancies ending in miscarriage or stillbirth and those with iatrogenic delivery before 34 weeks. The commonest causes of iatrogenic PTD in our cohort were PE and fetal growth restriction. In the investigation of the relationship between racial origin and iatrogenic PTD, we excluded pregnancies ending in miscarriage or stillbirth and those with spontaneous delivery before 34 weeks.

SGA and LGA neonates were defined as those with birth weight below the 5th percentile or above the 95th percentile for gestation, respectively. In the investigation of the relationship between racial origin and SGA or LGA, we excluded pregnancies ending in miscarriage or fetal death before 24 weeks.

Emergency CS included all cases where such delivery was undertaken after the onset of labor, usually for failure to progress, fetal distress or intrapartum hemorrhage. This group also included cases of antepartum hemorrhage requiring CS. Elective CS was performed before the onset of labor for obstetric or medical indications, or at the request of the mother. In the investigation of the relationship between racial origin and elective or emergency CS, we excluded pregnancies ending in miscarriage or fetal death before 24 weeks.

Statistical analysis

Univariable logistic regression analysis was performed to examine the association between racial origin and each of the adverse pregnancy outcomes. The risk for each of the pregnancy outcomes was then calculated from the formula: odds/(1 + odds), where odds = e^Y, and Y was derived from the univariable logistic regression analysis. Multivariable logistic regression analysis was performed for the prediction of each pregnancy outcome from racial origin, maternal age, weight, height, mode of conception, smoking, history of chronic hypertension or diabetes, history of adverse outcome in a previous pregnancy or family history of PE. Before performing the multivariable regression analysis, continuous variables were centered by subtracting the mean from each measured value (69 from maternal weight in kg, 1.64 from maternal height in meters and 30 from maternal age in years).

The statistical software package SPSS Statistics 18.0 (SPSS Inc., Chicago, IL, USA) was used for data analyses.

RESULTS

During the study period, first-trimester combined screening for aneuploidies was carried out in 79 694 singleton pregnancies. We excluded 3533 (4.4%) cases from further analysis because there were no or incomplete data on pregnancy outcome (n = 2407), because of the prenatal or postnatal diagnosis of aneuploidy or major defect.
or because of pregnancy termination for psychosocial reasons (n = 1126).

In the remaining 76 161 singleton pregnancies, there were 75 104 live births, 764 (1.0%) miscarriages and 293 (0.4%) stillbirths. In three of the stillbirths, fetal death was the consequence of maternal death (car accident in two and eclampsia in one), and these were excluded from further analysis.

In the 76 158 cases included in the study, the racial origin was Caucasian in 57 564 (75.6%), Afro-Caribbean in 11 395 (14.9%), South Asian in 3645 (4.8%), East Asian in 1793 (2.4%) and mixed in 1761 (2.3%). The median maternal age was 31.3 (range, 14.3–55.3) years, median height was 164 (range, 131.1–198.1) cm and median weight was 65.4 (range, 35–172) kg, 7651 (10.0%) women were cigarette smokers, 870 (1.1%) had a history of diabetes Type 1 or Type 2.

The results of multivariable logistic regression analysis for the prediction of miscarriage, stillbirth, PE, GH, GDM, delivery of an SGA or an LGA neonate and elective or emergency CS from racial origin, maternal age, weight and height, mode of conception, smoking, history of chronic hypertension or diabetes and previous obstetric history are summarized in Tables S1–S5 online. The odds ratios obtained from the multiple logistic regression analyses demonstrating association of maternal racial origin with pregnancy complications after adjustment for confounding factors in obstetric history and maternal characteristics are shown in Table 2.

Multiple logistic regression analysis demonstrated that, in women whose pregnancy was complicated by miscarriage, there were significant contributions from Afro-Caribbean and mixed racial origin, maternal age, height and weight, assisted conception using ovulation drugs, cigarette smoking, chronic hypertension and Type 2 diabetes. There was no significant contribution from other racial groups, maternal age, assisted conception using in-vitro fertilization (IVF) or Type 2 diabetes (Tables 2 and S1). In the prediction of stillbirth, there were significant contributions from Afro-Caribbean racial origin, maternal weight and height, assisted conception using ovulation drugs, cigarette smoking, chronic hypertension and Type 1 diabetes. There were significant contributions from other racial groups, maternal age, assisted conception using ovulation drugs, cigarette smoking, chronic hypertension and Type 1 diabetes. There was no significant contribution from other racial groups, maternal age, assisted conception using IVF, chronic hypertension, Type 1 diabetes, previous PE and a family history of PE (Tables 2 and S2).

In the prediction of GH, there were significant contributions from Afro-Caribbean racial origin, maternal age, weight and height, cigarette smoking, previous PE and a family history of PE (Tables 2 and S2).

Risk factors for SGA neonates included all non-Caucasian racial origins, conception using ovulation drugs, smoking, chronic hypertension, Type 2 diabetes.
Race and pregnancy complications

Figure 1 Forest plot of odds ratios with 95% CI, after adjustment for maternal characteristics and obstetric history, for the risk of pregnancy complications in women from Afro-Caribbean racial origin compared with Caucasians.

Table 2 Odds ratios obtained from multiple logistic regression analysis demonstrating association of maternal racial origin with pregnancy complications after adjustment for confounding factors in obstetric history and maternal characteristics

<table>
<thead>
<tr>
<th>Pregnancy complication</th>
<th>Afro-Caribbean</th>
<th>South Asian</th>
<th>East Asian</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal loss</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Miscarriage ((n = 764))</td>
<td>3.18 (2.70–3.74)</td>
<td>1.31 (0.91–1.89)</td>
<td>1.13 (0.66–1.93)</td>
<td>2.46 (1.68–3.60)</td>
</tr>
<tr>
<td>Stillbirth ((n = 290))</td>
<td>2.38 (1.82–3.11)</td>
<td>1.10 (0.61–1.99)</td>
<td>0.58 (0.18–1.82)</td>
<td>1.10 (0.49–2.48)</td>
</tr>
<tr>
<td>Pre-eclampsia ((n = 1698))</td>
<td>2.60 (2.32–2.92)</td>
<td>1.73 (1.39–2.15)</td>
<td>1.11 (0.77–1.60)</td>
<td>1.30 (0.93–1.81)</td>
</tr>
<tr>
<td>Gestational hypertension ((n = 1807))</td>
<td>1.39 (1.23–1.57)</td>
<td>1.16 (0.92–1.46)</td>
<td>0.86 (0.60–1.25)</td>
<td>0.96 (0.69–1.64)</td>
</tr>
<tr>
<td>Preterm delivery (&lt;34) weeks</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Spontaneous delivery ((n = 768))</td>
<td>1.94 (1.63–2.32)</td>
<td>1.36 (0.99–1.87)</td>
<td>0.87 (0.51–1.49)</td>
<td>1.44 (0.94–2.22)</td>
</tr>
<tr>
<td>Iatrogenic delivery ((n = 513))</td>
<td>2.78 (2.22–3.49)</td>
<td>1.70 (1.12–2.59)</td>
<td>0.92 (0.43–1.98)</td>
<td>1.89 (1.08–3.31)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective Cesarean section ((n = 8785))</td>
<td>0.87 (0.81–0.93)</td>
<td>1.08 (0.97–1.20)</td>
<td>0.93 (0.80–1.09)</td>
<td>0.86 (0.73–1.01)</td>
</tr>
<tr>
<td>Emergency Cesarean section ((n = 10 738))</td>
<td>1.49 (1.41–1.58)</td>
<td>1.22 (1.10–1.34)</td>
<td>1.00 (0.87–1.15)</td>
<td>0.98 (0.85–1.13)</td>
</tr>
</tbody>
</table>

Comparison of each maternal racial origin group was with those of Caucasian racial origin. Data are given as odds ratio (95% CI). BW, birth weight; LGA, large-for-gestational age; SGA, small-for-gestational age.
mellitus and maternal age (Tables 2 and S3). Maternal height, multiparity and Type 1 diabetes mellitus were associated with reduced risk. Whilst maternal age, weight and height, pre-existing diabetes and multiparity were associated with an increased risk of delivering an LGA neonate, Afro-Caribbean, South Asian and mixed racial origins, smoking and chronic hypertension were associated with reduced risk (Tables 2 and S3). Women of Afro-Caribbean, South Asian and East Asian racial origins were more likely to develop GDM (Tables 2 and S3). Maternal age and weight, and conception using ovulation drugs, were associated with an increased risk of GDM, whilst maternal height was protective.

In the prediction of spontaneous PTD, there were significant contributions from Afro-Caribbean racial origin, assisted conception, smoking and pre-existing diabetes mellitus. Taller women were less likely to experience spontaneous PTD (Tables 2 and S4). The risk factors for iatrogenic PTD included Afro-Caribbean, South Asian and mixed racial origins, assisted conception, smoking and pre-existing diabetes mellitus, chronic hypertension and maternal weight (Tables 2 and S4). Taller and parous women were less likely to experience iatrogenic PTD.

Risk factors for emergency CS included Afro-Caribbean and South Asian racial origins, maternal age and weight, smoking, chronic hypertension, pre-existing diabetes mellitus and conception using IVF (Tables 2 and S5). Taller and parous women were less likely to have an emergency CS. Afro-Caribbean women and smokers were less likely to have elective CS, whilst those who conceived using IVF, had pre-existing diabetes mellitus or were parous were more likely to have elective CS (Tables 2 and S5). Maternal age and weight were associated with an increased chance of having an elective CS, whilst maternal height was associated with a reduced chance.

**DISCUSSION**

The results of our study demonstrate that, after accounting for potential confounding variables, there remains a significant association between maternal racial origin and a wide range of adverse pregnancy outcomes. In Afro-Caribbean women, compared with Caucasians, there was a higher prevalence of miscarriage, stillbirth, PE, GH, SGA, spontaneous and iatrogenic PTD and emergency CS. South Asian racial origin was associated with increased risk for GDM, PE, SGA, iatrogenic PTD and CS, and East Asian race had increased risk for GDM and SGA.

The strengths of our study include the large number of subjects, the diverse racial origin of our population, accurate assessment of gestational age and recording of maternal weight and height, examination of a large number of adverse pregnancy outcomes, prospective collection of data and the use of multivariable logistic regression analysis to control for risk factors associated with each adverse outcome. A limitation of the study is the lack of data on level of education and socio-economic class of the women.

In this study the patients were recruited at 11+0 to 13+6 weeks of gestation when the fetuses were demonstrated to be alive. Consequently, we examined the rate of second-trimester, rather than total, miscarriage. Essentially there are two broad categories for second-trimester miscarriage: fetal death caused by extreme placental impairment; and extremely early spontaneous delivery of a fetus that dies during labor and/or delivery. In this respect, miscarriage could be considered to represent the extreme end of the spectrum of impaired placentation, with the associated PE, SGA and stillbirth, and spontaneous PTD, which are also increased in women of Afro-Caribbean racial origin, compared with Caucasians.

The rate of stillbirth in women of Afro-Caribbean origin is twice as high as in Caucasians and this is compatible with the results of national statistics. A study of 5 138 122 singleton pregnancies from the US National Center of Health Statistics reported that the risk of stillbirth at 20–23 weeks’ gestation was 2.8-times higher, and the risk of death at 39–40 weeks was 1.6-times higher, in women of Afro-Caribbean racial origin when compared with Caucasian women. The Confidential Enquiries into Maternal and Child Health in the UK reported that the rate of stillbirth in women of African racial origin was 2.3-times higher than in Caucasian women. This increased risk of stillbirth in Black women has been attributed to late access to prenatal care, low level of education and previous stillbirth. In our study all women booked early for prenatal care and had equal access and quality of care within the National Health System. The increased risk of stillbirth in Afro-Caribbean women is likely to be secondary to their higher prevalence of PE, SGA and GDM.

The rates of both spontaneous and iatrogenic PTD were two to three times higher in Afro-Caribbean women than in Caucasian women. In the USA national vital statistics in 2005, the PTD rate was 18.4% in Afro-Caribbean women compared with 11.7% in Caucasian women. The majority of previous studies examining the association between PTD and maternal racial origin defined PTD as that occurring prior to 37 weeks’ gestation. However, PTD < 34 weeks is more relevant to current obstetric practice as neonatal morbidity and mortality are substantially less after this gestation. We examined spontaneous and iatrogenic PTD as separate outcomes, owing to differences in their risk factors, pathogenesis and management. In our study cohort the risk factors for iatrogenic PTD overlap with those for PE and SGA. This is expected as the majority of women in the iatrogenic PTD group had PE and/or SGA. A population-based study of 585 291 singleton pregnancies from the UK has shown that, after correcting for other confounders, the rate of spontaneous PTD < 37 weeks in women of Afro-Caribbean racial origin, compared with Caucasian women, was higher by a factor of 1.6. The most commonly postulated causes of spontaneous PTD, including urogenital infection and short cervical length, are more common in Afro-Caribbean women compared with other racial groups.

The rate of PE was higher in women of Afro-Caribbean and South Asian racial origin, compared with Caucasian women. These racial differences are also observed in non-pregnant subjects, both in terms of metabolic profiles.
and susceptibility to different types of cardiovascular disease. In both Afro-Caribbean and South Asian populations the prevalence of chronic hypertension and cardiovascular disease are increased, but Black individuals are more susceptible to stroke and end-stage renal failure, and people of South Asian origin to coronary heart disease. According to our findings, Afro-Caribbean race was the second strongest risk factor for PE after chronic hypertension. For this reason, we believe that racial origin should be incorporated into PE risk assessment and planning for further antenatal care. The UK national guideline for the management of hypertension in pregnancy suggests a list of risk factors, including advanced maternal age and family history of PE, but not racial origin, that increase the risk of PE and for which low-dose aspirin should be prescribed from 12 weeks' gestation. Our data demonstrate that Afro-Caribbean race is a stronger risk factor for PE than are advanced maternal age or family history of PE.

In women of Afro-Caribbean and South Asian racial origin the rate of SGA neonates was higher, and that of LGA neonates was lower, than in Caucasian women. Our results are in general agreement with those of previous studies. In defining fetal growth we used a reference range of birth weight for gestational age for our population in which the majority of women were Caucasian. In this reference range we did not make adjustments for racial origin because, in women living in western societies, such adjustments could mask pathologic influences. As demonstrated in our study in women of Afro-Caribbean racial origin, there is an increased risk of several adverse pregnancy outcomes, including stillbirth, even after adjustment for demographic and pregnancy characteristics.

The incidence of GDM was significantly higher in Afro-Caribbean and Asian women compared with Caucasian women, with the highest risk seen in Asian women. This association is consistent with the literature where several studies have reported a similar finding. Compared with Caucasian women, racial minorities are at a higher risk of pre-existing diabetes, which could be revealed for the first time during pregnancy as apparent GDM. The increased risk of GDM in non-Caucasian women might also be a reflection of their higher background risk of developing diabetes in general, beyond what is accounted for by obesity. Recognizing this racial disparity in the risk of developing GDM, the UK national guideline for the management of diabetes in pregnancy recommends routine screening for GDM for all Afro-Caribbean and South Asian women. The racial differences could be explained by genetic variation, lifestyle or cultural factors. Consistent with other studies, the risk of CS in our study population was significantly higher in women of Afro-Caribbean and South Asian racial origin. This racial difference persisted even after adjusting for potential confounding variables, known to be risk factors, such as maternal age, socio-economic status, pre-existing chronic disease and obstetric complications such as PE and macrosomia. Other variables that could explain this disparity, not accounted for in most studies, include patient preference, biological factors that increase the risk of non-reassuring intrapartum fetal monitoring in some populations and provider bias in the Cesarean delivery rate.

In order to formulate an individualized patient- and disease-specific risk assessment, algorithms derived from multivariable logistic regression analysis, which combine maternal racial origin with other maternal and pregnancy factors, are required. This could lead to a new approach to antenatal care, whereby the patient-specific risk for a wide variety of pregnancy complications is estimated at a first hospital visit at 11–13 weeks' gestation and more targeted antenatal surveillance and intervention can be planned. As demonstrated in this study, maternal racial origin has a strong influence for most major pregnancy complications.

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**SUPPORTING INFORMATION ON THE INTERNET**

The following supporting information may be found in the online version of this article:

- **Table S1** Multivariable logistic regression analysis for the prediction of miscarriage and stillbirth by maternal factors and obstetric history.
- **Table S2** Multivariable logistic regression analysis for the prediction of pre-eclampsia and gestational hypertension by maternal factors and obstetric history.
- **Table S3** Multivariable logistic regression analysis for the prediction of small- and large-for-gestational age neonates and gestational diabetes by maternal factors and obstetric history.
- **Table S4** Multivariable logistic regression analysis for the prediction of spontaneous and iatrogenic preterm delivery before 34 weeks’ gestation by maternal factors and obstetric history.
- **Table S5** Multivariable logistic regression analysis for the prediction of elective and emergency Cesarean section by maternal factors and obstetric history.