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Analysis of routinely collected data: Determining associations of maternal risk factors and infant outcomes with gestational diabetes, in Pakistani, Indian, Bangladeshi and white British pregnant women in Luton, England.

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Conflict of Interests

The authors declare that there are no competing interests.

Ethics approval

Ethics approval was provided by [removed], (removed).

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Authors Contributions

RG and NA conceived the study; MG assisted with identification of data, RG and AG conducted the statistical analyses, RG, GR, AG, MG and NA contributed to earlier drafts of the manuscript and all authors approved the final version.

Objective

This study aims to compare the prevalence of gestational diabetes in Indian, Pakistani, Bangladeshi and British women in Luton, England and further examine associations in maternal risk factors (age BMI, smoking status and birth outcome), with gestational diabetes, with maternal ethnicity.

Design

A retrospective analysis using routinely collected secondary data from Ciconia Maternity information System (CMiS), between 2008 and 2013. The ethnicity of women recorded as Indian, Pakistani, Bangladeshi and white British, residing in [removed] were included in the study. The outcomes for n=15,211 cases were analysed using adjusted standardised residuals, Pearson Chi-square, frequencies and percentages of women with gestational diabetes.

Results

The prevalence of gestational diabetes was significantly higher in the sample of Bangladeshi (2.1%) and Pakistani (1.4%) compared to Indian (1%) and white British (0.4%) women. Of the women diagnosed with gestational diabetes, 48.7% of the women diagnosed with gestational diabetes in this cohort were Pakistani, compared with 28.3% of Bangladeshi, 6.6% of Indian and 16.4% of white British ($\chi 2= 84.57$ df=6, $p<0.001$). A number of significant Pearson Chi-square associations were found between Pakistani women diagnosed with gestational diabetes and BMI over 30kg/m^2 (χ^2= 43.1 *df*=4, *p*<0.001) and an early gestational age at delivery (24-37 weeks) ($\chi 2$= 4.084 *df*=1, *p*=0.043).

Conclusions

There are important differences in the prevalence rates of gestational diabetes which varied by maternal ethnicity. Of the women who had GDM, 48.7% were Pakistani, compared with 28.3% Bangladeshi, 16.4% white British and 6.6% Indian. It is essential policy makers and service providers target GDM screening and associated interventions and future research seeks to understand the reasons behind these differences.

Introduction

Gestational diabetes (GDM) is associated with adverse pregnancy outcomes (The HAPO Study Cooperative Research Group, 2008; World Health Organization, 2013) including macrosomia (Evers, de Valk, & Visser, 2004; Kenny et al., 2013), congenital anomalies (Sheridan et al., 2013) and perinatal mortality (Eidem et al., 2011; Macintosh et al., 2006). Risks continue after delivery, where women are at higher risk of developing type II diabetes, whilst evidence suggests that infants have an increased risk of becoming obese and developing insulin dysfunction in adulthood (Barker, 1995; Lawlor, Lichtenstein, & Långström, 2011).

The prevalence of GDM is currently estimated to affect 5% of pregnancies, increasing to 30% if the mother has previously suffered from GDM (Diabetes UK, 2015), and varies between mothers from different ethnic groups. Research has shown that South Asian women are at increased risk of developing GDM (Bryant et al., 2014; Makgoba, Savvidou, & Steer, 2012). This is also consistent with the trend that South Asians have a higher propensity to develop DM across the life course (Farrar et al., 2015). Explanations for the higher risk in South Asians include genetic predisposition and lifestyle factors and the fetal origins hypothesis, which considers the contribution of low birthweight and the later development of metabolic dysfunction (Barker, 1995; Gracelyn & Saranya, 2016).

There is a growing body of evidence on GDM, but few studies have been published on GDM in ethnic minorities (Hernandez-Rivas et al., 2013; Mocarski & Savitz, 2012; Sanchalika & Teresa, 2015). Despite this, there are only two UK based studies that have examined the prevalence of GDM comparing South Asian and white European/British pregnant mothers. Using retrospective data which included over 15,000 pregnancies from South Asian women across North West London, Makgoba *et al* (2012) demonstrated that GDM had a higher prevalence South Asian women (1.9%) compared with white European women (0.7%), of which more South Asian women (25%) required insulin treatment in comparison to white European women (14.7%) (Makgoba et al., 2012). This suggests that optimal blood glucose levels are not clinically achieved in South Asian women during pregnancy, without intervention. This may be a consequence of poor lifestyle and dietary management, low adherence to pharmacotherapy, poor treatment response or a combination of these and other factors.

The Born in Bradford (BiB) cohort study has also published prevalence rates for diabetes (DM) in white British and South Asian women, however, their results showed similar rates between Pakistani and white British women and have not included Bangladeshi or Indian mothers. The BiB results for DM ranged from 3-5%, (Sheridan et al., 2013), which were slightly lower to recently published national figures (i.e. 5% for GDM and 6.2% for DM - UK average) (Diabetes UK, 2015). Luton, where this study is based, has a plural population with a high proportion of

Black Asian and Minority Ethnic (BAME) residents, where the Pakistanis and Bangladeshi community account for one-fifth of the town's residents (Geospatial Information Team & Department of Environmental and Regeneration, 2014; Mayhew & Waples, 2011). Furthermore, figures show that in England, Pakistani and Bangladeshi have worse birth outcomes than White British women (Office for National Statistics, 2014; Taylor & Harrison, 2013), so unsurprisingly, Luton has a high rate of perinatal mortality in the East of England.

Prevalence rates across individual studies vary, as a consequence of researchers focusing on pre-existing DM (type I or II) or GDM (Carolan, 2013). Furthermore, the lack of consensus in clinically relevant diagnostic thresholds has also contributed to heterogeneity between studies and subsequent research outcomes (Ferrara, 2007). For instance, in the UK, GDM is diagnosed with a fasting plasma glucose level of >5.6mmol/l, however following the publication of the consensus guidelines in managing GDM (The HAPO Study Cooperative Research Group, 2008), clinical guidance was revised and GDM diagnosis is also now given with a 2-hour plasma glucose level is found to be > 7.8mmol/l (National Institute for Health and Clinical Excellence (NICE), 2015). Moreover, in the UK, screening for diabetes is not universal to all pregnant women and pre-identified risk factors are used to determine whether to offer screening for diabetes, namely; BMI >30kg/m2, previous GDM, previous macrosomic infant, family or first degree relative with diabetes, ethnic minority family with a history of diabetes (National Institute for Health and Clinical Excellence (NICE), 2015). Consequently, it is possible that some women remain undiagnosed, dependant on the screening policy in individual NHS trusts.

Another important limitation to previous research is the Sample sizes of South Asian populations which is varied, and often Indian, Pakistani and Bangladeshi women are aggregated into one homogenous group or alternatively the ‘South Asian’ category has been used to reported findings that are specific to Pakistanis (Sheridan et al., 2013). Consequently, important differences (and similarities) in the prevalence of diabetes (including GDM) between Indian, Pakistani and Bangladeshi women remain under researched. The aim of this study is to compare the prevalence of GDM in Indian, Pakistani, Bangladeshi and white British women and examine other stratified maternal risk factors and infant outcomes with GDM.

Methods

Retrospective, routinely collected secondary data from the Ciconia Maternity information System (CMiS) was accessed from the XXXXXX hospital NHS Foundation Trust. Purposive sampling of women aged over 16 who delivered their infant between January 2008 and December 2013 and who resided in specific postcode areas was used to ensure a geographically homogenous sample.

Variables:

Following a review of the existing literature, data for the following variables were identified and extracted; singleton or multiple, marital status, maternal age, booking date, parity, smoking status, diabetes, hypertension, maternal height, maternal weight (at booking), BMI, maternal ethnicity, birth outcome, infant birthweight, delivery method and infant gender (Cresswell et al., 2013; Freemantle et al., 2009; Kim & Saada, 2013; Ravelli et al., 2011; Yadav & Lee, 2013). This formed a larger data set, which was used for a wider study [reference removed for per review]

GDM screening was conducted within the hospital sample following National Institute for Health and Care Excellence (NICE) guidelines, therefore offering all South Asian women GDM screening, and only offering screening to white British women, identified at high risk of GDM (National Insitute for Health and Care Excellance, 2014; The National Institute for Health and Care Excellence, 2016). This data uses self-ascribed ethnic codes, which are part of the NHS mandatory data set; coded according to the 2001 census categories (Department of Health, 2008).Ethnicity is a self-defined construct, which incorporates culture, religion, shared language and ancestry (Economic and Social Data Service, 2012). Therefore, maternal country of birth, generational status and length of residency is not accounted for. Only results for white British, Indian, Pakistani and Bangladeshi women are reported in this paper, using white British as a comparator.

Ethic approval was provided by the [removed for peer review] Research Ethics Committee (March 2014) and approval was given by the [removed for peer review] NHS Trust Research and Development department and the Hospitals Information Governance Manager ensured adherence to patient confidentiality and data protection before de-identified routinely collected data was provided.

Statistical analysis:

Analyses were conducted using IBM Statistics Package for the Social Sciences (SPSS) ® v21. The raw data was separated; so that only Indian, Pakistani, Bangladeshi and white British women's outcomes are reported in this paper. A number of variables were transformed: birth outcome (as a binary variable: live/dead) (n= 15 211), maternal BMI (<18.5-18.9, 19-24.9, 25-

29.9, 30-39.9, 40-60)(n= 15,203), maternal age[1] (≤ 20; 21-25; 26-30; 31-35; 36-40; ≥ 41), gestation age at delivery (24-37, >37 weeks of gestation), and smoking status (binary variable, yes/no) and gestational diabetes was coded as a binary variable (yes/no), after being separated from the other diabetes data codes (i.e. pre-existing diabetes, insulin dependent and non-diabetic) within the raw data.

Frequency counts and percentages, in addition to Cross-tabulations, adjusted standardised residuals (ASR) and Pearson Chi-square was used to determine whether there were any significant associations between maternal ethnicities and maternal characteristics.

Results

This paper reports the prevalence and characteristics of GDM of Indian, Pakistani, Bangladeshi and white British mothers. There was a total of 15,211 data entries in CMiS for 2008-2013. From this, 152 women had a diagnosis code for GDM. Cases with missing data were excluded. Missing data was as follows: diabetes diagnosis code n=69 (all codes), maternal age n=1, smoking n=29, BMI standard n=8, birth outcome n=0, gestation age at delivery n=34).

The cohort characteristics are shown in table 1. This shows that 152 women had GDM, and the most frequent age range for having GDM was 31-35 years (37.5%), compared with 0.7% of mothers aged 16-20 years. The data also shows that 93.1% of smokers were white British, and 48.2% of preterm deliveries were also from mothers who were white British. Conversely, Bangladeshi (1.1%) and Pakistani (1%) women had proportionally higher stillborn infants than

[1] Due to de-identifying the CMiS data, age was provided in age ranges

white British (0.7%) mothers and 8.1% of Pakistani women had a BMI (standard BMI metrics) recorded between 40-60kg/m^2, compared with 0.8% of Indian mothers.

[table 1]

Table 2 shows the frequency and percentage of women, stratified by maternal ethnicity, that have GDM, DM or non-diabetes. The overall prevalence of GDM within the cohort was 1% (n=152), but the prevalence varied by maternal ethnicity. Of the women who had GDM, 48.7% were Pakistani, compared with 28.3% Bangladeshi, 16.4% white British and 6.6% Indian. Conversely, Pakistani women made up 33.8% of the sample size, compared with 42.6% of white British women.

[table 2 here]

Pearson chi-square were calculated to determine whether there were any significant associations between women (stratified by ethnicity) diagnosed with GDM and maternal characteristics (i.e. BMI, maternal age, birth outcome, smoking status and gestation age at delivery). Significant associations were found between maternal ethnicity and diagnosis of GDM: Pakistani and Bangladeshi women were overrepresented (compared to chance) having a diagnosis of GDM (ASR = 3.9, ASR = 5.4) conversely, white British women were overrepresented (compared with chance) not having a diagnosis of GDM (ASR = 8.0) ($\chi 2$= 84.57 *df*=6, *p*<0.001).

There were a number of significant trends in the age data. White British (ASR= 4.1, ASR = 2.8) and Pakistani women with GDM were over represented in 36-39 years (ASR = 2.0, $\chi2$= 26.49*df*=5, *p*<0.001) and over 40 years (ASR = 3.2, (, $\chi2$= 46.66*df*=5, *p*<0.001) age bands. Indian (ASR = 3.1, $\chi2$= 9.85 *df*=5, *p*=0.08) and Pakistani (ASR = 4.8, $\chi2$= 46.66 *df*=5, *p*<0.001) women with GDM were over represented in the age band 31-35 years. Pakistani (ASR = -3.8, $\chi2$= 46.66 *df*=5, *p*<0.001) and Bangladeshi (ASR = -2.5, $\chi2$= 13.86 *df*=5, *p*=0.017) women diagnosed with GDM were under represented in age bands 21-25 years.

Individually by ethnic groups, the results for smoking status and GDM were not significant, but when all 4 ethnic groups were combined, non-smoking status and GDM showed a significant association (ASR = 2.7, $\chi2$= 7.29 *df*=1, *p*=0.007). There were no significant associations found between maternal ethnicity, GDM and birthweight (<1499g, 1500-2499.99g, >2500g) or birth outcome (as a binary variable live/dead). However, significant associations were found in GDM and pre-term delivery (24-37 weeks of gestation) but only with Pakistani women (ASR = 2, $\chi2$= 4.084 *df*=1, *p*=0.043).

A Chi-square test of association was conducted between GDM, ethnicity and BMI (<18.5, 19-24.9, 25-29.9, 30-39.9, 40-60) (figure 1). Several significant associations were identified: white British, Pakistani and Bangladeshi women were underrepresented in 19-24.9kg/m^2 (ASR = -2.5, χ^2= 43.1 *df*=4, *p*<0.001, ASR = -3.4, χ^2= 21.04 *df*=4, *p*<0.001, ASR = -2.6, χ^2= 46.23 *df*=4, *p*<0.001, respectively), and over represented in BMI groups over 30kg/m^2 (ASR = 4.7, χ^2= 43.1 *df*=4, *p*<0.001, ASR = 3.4, , χ^2= 21.04 *df*=4, *p*<0.001, ASR =5.6, χ^2= 46.23 *df*=4, *p*<0.001, respectively) and white British and Bangladeshi women were over represented in BMI groups

$40kg/m^2$ (ASR = 4.1, χ^2= 43.1 *df*=4, *p*<0.001, ASR = 3.5, χ^2= 46.23 *df*=4, *p*<0.001). Cramers *V* = .221 and showed that the effect size was moderate.

Discussion

This paper uses routinely collected maternity data over six years and shows important differences in the prevalence of risk factors for adverse birth outcomes, including GDM *between* Indian, Pakistani and Bangladeshi and White British ethnicity, in [removed] England. Pakistani women were the largest proportion of women diagnosed with GDM within this cohort, although Bangladeshi women have the highest prevalence within their ethnic group, compared to white British, Pakistani and Indian women. This study also found both the overall prevalence of GDM and the prevalence specifically in South Asian women was lower than previous published results in the BiB cohort (3-5%)(Sheridan et al., 2013), and Makgoba and colleagues (1.9%) (2012), in addition to being lower than national estimates (5%) (Diabetes UK, 2015).

The results revealed a number of significant associations between maternal characteristics which were stratified by ethnicity and GDM diagnosis categories. For instance, Pakistani women with GDM were significantly over represented in the category of early deliveries (between 24-37 weeks of gestation). However, this is contradictory to the previous findings from Makgoba and colleagues (2012), who found no difference between white European and South Asian women with GDM and gestation age at delivery. Furthermore, these results showed that Pakistani women with GDM were also over represented in the BMI group over $30kg/m^2$, whereas Makgoba and colleagues (2012) found that South Asian women had a lower BMI than white European women. Nevertheless, this may be the consequence of a methodological artefact; a result of the population demographics, but this is difficult to establish as the authors used data from the Health Improvement Network (THIN) database and have not explicitly specified maternal ethnicity (i.e. Indian, Pakistani or Bangladeshi), in order to understand the proportion of each ethnicity contained within their broad classification of South Asian. For example, if Makgoba *et al's* study data included South Asian women from practices based in East London, 32% of the population are recorded as being Bangladeshi whereas only 1% are Pakistani and 2% Indian (Tower Hamlets Council, 2013), whereas in this study Bangladeshi women constitute 13.5% of the cohort.

This analysis also found that Pakistani women had the highest percentage of women with GDM within all women in this cohort (i.e. those with GDM and no diagnosis), and those with GDM were also over represented in the BMI group 30kg/m^2 and 40kg/m^2. Conversely, white British women had the lowest prevalence of GDM, women with GDM were also found to be over represented in BMI groups 30kg/m^2 and 40kg/m^2. The linear relationship of the development of DM and corresponding increasing BMI is well documented, (Coton, Nazareth, & Petersen, 2016; Hernandez-Rivas et al., 2013) however, GDM is not (Sebire et al., 2001) and there is clearly a difference in the diagnosis of GDM and maternal ethnicity.

Maternal ethnicity, diagnosis of GDM and age also showed significant associations. Specifically, white British and Pakistani women with GDM were over represented in age bands over 36, whereas Pakistani and Bangladeshi women with GDM were under represented in age band 21-25. This trend is consistent with previous findings that have shown older maternal age and GDM has a linear relationship (Ferrara, 2007; Metzger, 2010). Interestingly, Indian women had no significant associations in any of the maternal characteristics in this study, which warrants further investigation.

This paper advances knowledge on several important findings. There are clear differences in the prevalence of GDM *between* South Asian women, showing that both Pakistani and Bangladeshi women have a much higher prevalence of GDM compared with Indian or white British women, in addition to differences in prevalence between Pakistani and Bangladeshi women.

This is the first paper that we are aware of to publish the prevalence of GDM *between* south Asian women in the UK, showing trends that contradict and extend our previous knowledge of the prevalence of GDM in south Asian women, showing discerning patterns in the data between Pakistani, Bangladeshi and Indian women which will have implications on managing their risk in practice. The strengths of this work includes utilising six years of raw data from a town with a diverse population which includes high numbers of south Asian settlers, resulting in a large sample size of Pakistani, Bangladeshi, Indian women. In addition, the data comes from a single hospital unit, meaning there would be consistency in the locality for screening and management for GDM, unlike larger studies who utilise data from a wider geographic area of data sites, such that homogeneity of clinical practice is less likely and may impact the numbers of women diagnosed with GDM (Carolan, 2013; Makgoba et al., 2012). Nevertheless, it is understood that due to changes in the national guidance on the diagnosis and treatment of GDM during the period of the data used in this study, the diagnostic criteria (i.e. methods and thresholds) may have changed (National Institute for Health and Care Excellence, 2015; NICE (National Insitute for Health and Care Excellance), 2014). Consequently, year on year comparisons are not possible. Furthermore, while accepting the diagnostic criteria of screening women from South Asian origin for diabetes during pregnancy, may have skewed the results of this paper, it does lead to the question whether some women remain undiagnosed.

Nevertheless, there are some limitations. The accuracy of these results depends on the accuracy of data input within the CMiS system. Typically, midwives enter the data in the system, whereby errors may occur when transposing data from paper records. Furthermore, the code 'pre-existing diabetes' is predetermined data entry code in CMiS and therefore we were unable to differentiate between DM1 and DM2 within this cohort. Future studies may want to discern whether DM1 is more equally prevalent in Indian, Pakistani and Bangladeshi expectant mothers, given that recent evidence shows genetic and environmental contributory factors which are likely to affect South Asian settlers (Pociot & Lernmark, 2016; Rewers & Ludvigsson, 2016). Due to using pre-existing data, which used the NHS ethnic codes, we were unable to discern whether length of residency or country of birth mediated any of the outcomes reported in this paper. It would be useful for future studies to consider this further.

Implications for policy or practice

The findings from this study have important implications for policy and practice. This paper shows an over-representation of Pakistani and Bangladeshi mothers with GDM, compared to Indian mothers, while white British mothers were significantly under-represented for GDM, however more white British mothers had a BMI >40kg/m^2. This highlights the need for targeted interventions according to risk, whereby clinicians can offer culturally appropriate lifestyle advice in respect of GDM, healthy eating, exercise advice early in a woman's family planning, pre-conception and pregnancy journey, as opposed to on diagnosis of GDM.

Furthermore, the cessation of collating data on South Asian women as one homogenous group is also necessary as this obscures nuanced and salient differences (Garcia, Ali, Papadopoulos, & Randhawa, 2015). By understanding which groups of people are at most risk for developing GDM, careful surveillance and lifestyle interventions can be implemented much earlier during the pre-conception and antenatal care pathway to help minimise adverse outcomes, Further research is needed to understand what lifestyle factors may contribute to the findings in this paper, such that Indian women have a significantly lower prevalence of GDM and to determine why GDM Pakistani women deliver their infants earlier than Indian or Bangladeshi or white British women.

Conclusion

In conclusion, this paper demonstrates a higher prevalence of GDM Pakistani and Bangladeshi women compared with Indian and white British mothers, and provides evidence for heterogeneity within the ethnic classification of 'south Asian' (Makgoba et al., 2012). Additionally, the results of this study show that Pakistani mothers with a disproportionate diagnosis of diabetes in pregnancy, which warrants further attention.

List of Abbreviations

Ciconia Maternity information System (CMiS)

Gestational diabetes (GDM)

United Kingdom (UK)

Born in Bradford (BiB)

Diabetes mellitus (DM)

National Health Service (NHS)

Body mass index (BMI)

National Institute for Health and Care Excellence (NICE)

Statistics Package for the Social Sciences (SPSS)

Adjusted standardised residuals (ASR)

Health Improvement Network (THIN)

Diabetes type 1 (DM1)

Diabetes type 2 (DM2)

Declarations

Ethics approval

Ethics approval was provided by [removed] Institute for Health Research, (IHRREC442, November 2014).

Consent for publication

Not applicable

Availability of data and material

The datasets generated and/or analysed during the current study are not publicly available due to potential identifiable information. For more information, please contact the corresponding author.

Competing Interests

The authors declare that there are no competing interests.

Funding

The Steel Trust has provided funding to ….[removed] .The funders have no involvement in the research undertaken or subsequent publications.

Authors Contributions

[removed]

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Table 1: Cohort characteristics, stratified by maternal ethnicity

Maternal ethnicity	GDM N (% of women with GDM)	GDM by Maternal age						Smokers N (% of smokers)	PTB n(%)		BMI n(%)					Birth outcome n(%)	
		16-20 years	21-25 years	26-30 years	31-35 years	36-40 years	over 40 years		24-36.9 weeks	37+ weeks	<18.5kg/m²	19-24.9 kg/m²	25-29.9 kg/m²	30-39.9 kg/m²	40-60 kg/m²	Live	stillborn
White British	25 (16.4)	1	4	5	5	8	2	1508 (93.1)	512 (7.3)	6493 (93.7)	1367 (19.5)	2540 (36.2)	1747 (24.9)	1173 (16.7)	188 (2.7)	6968 (99.3)	52 (0.7)
Indian	10 (6.6)	0	1	2	7	0	0	20 (1.2)	81 (8.2)	908 (92)	205 (20.7)	427 (43.1)	269 (27.1)	82 (8.3)	8 (0.8)	987 (99.6)	4 (0.4)
Pakistani	74 (48.7)	0	7	21	33	10	3	73 (4.5)	334 (6.5)	4796 (93.4)	1296 (25.2)	1644 (32)	1313 (25.5)	807 (15.7)	81 (1.6)	5090 (99)	53 (1)
Bangladeshi	43 (28.3)	0	5	20	12	5	1	18 (1.1)	135 (6.6)	1918 (93.4)	488 (23.7)	762 (37.1)	553 (26.9)	228 (11.1)	25 (1.2)	2034 (98.9)	23 (1.1)
Total (all women)	152 (100)	1 (0.7)	17 (11.2)	48 (31.6)	57 (37.5)	23 (15.1)	6 (3.9)	1619 (100)	1062 (6.9)	14115 (93)	3356 (22)	5373 (35)	3882 (26)	2290 (15)	302 (2)	15079 (99.1)	132 (0.9)

GDM – gestational diabetes, PTB – pre-term birth, BMI – Body Mass Index (kg/m²),

Table 2: Frequency and percentage of GDM, DM and non-diabetic diagnosis, stratified by maternal ethnicity.

Maternal ethnicity	GDM N (% of women)	DM N (% of women)	Non-diabetic N (% or women)	Total
White British	25(16.4)	29(28.7)	6938(46.6)	6992(42.6)
Indian	10(6.6)	4(4)	972(6.5)	986(6.5)
Pakistani	74(48.7)	43(42.6)	5006(33.6)	5123(33.8)
Bangladeshi	43(28.3)	25(24.8)	1973(13.3)	2041(13.5)
Total	152(100)	101(100)	14889(100)	15142(100)

GDM – gestational diabetes, DM - diabetes

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