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Are babies conceived during Ramadan born smaller and sooner than babies conceived at other times of the year? A Born in Bradford Cohort study

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Abstract

Background: It is not known whether infants exposed to intermittent maternal fasting at conception are born smaller or have a higher risk of premature birth than those who are not. Doctors are therefore unsure about what advice to give women about the safety of Ramadan fasting. This cohort study aimed to investigate these questions in Muslim mother-infant pairs to inform prenatal care.

Methods: Routinely collected data accessed from maternity records was the source of the data. Mothers were considered exposed if they were Muslim and Ramadan overlapped with their infant conception date, estimated to be 14 days after the last menstrual period. Infants were included as exposed if their estimated conception date was in the first 21 days of Ramadan or seven days prior to Ramadan.

Results: After adjusting for gestational age, maternal age, infant gender, maternal body mass index at booking, smoking status, gestational diabetes, parity and year of birth there was no significant difference in birth weight between infants born to Muslim mothers who were conceived during Ramadan (n=479) and those who were not (n=4,677) (adjusted mean difference=24.3 grams, 95% confidence interval=-16.4-64.9). There was no difference in rates of premature births in exposed and unexposed women (5.2% vs 4.9%; odds ratio=1.08, 0.71-1.65).

Conclusions: Healthy Muslim women considering becoming pregnant prior to, or during Ramadan, can be advised that fasting does not seem to have a detrimental effect on the size (weight) of their baby and it appears not to increase the likelihood of giving birth prematurely.

Keywords: Ramadan, premature birth, birth weight, born in Bradford, fasting.

What is already known-on this topic?

Muslim women planning to conceive a child will often ask their doctor or healthcare provider whether it is safe to fast during Ramadan but evidence on this question has been inconsistent.

What this study adds?

After taking account of gestational age and adjusting for important confounders, this study found that healthy Muslim infants conceived during Ramadan were not born smaller than Muslim infants conceived outside of Ramadan. Muslim women and their partners can be advised by doctors that Ramadan fasting around the time of conception appears unlikely to have a detrimental effect on the size of their infant at birth or result in premature birth.

Introduction

Every year Muslims fast for the entire month of Ramadan. While fasting from dawn until sunset Muslims refrain from consuming food and drinks, smoking, and engaging in sexual relations. Ramadan fasting can result in altered sleep patterns, acute and/or chronic hypohydration, altered mood, and changes to other lifestyle behaviours. Worldwide there are approximately 0.8 billion Muslim women of which 230 million are of child bearing age and globally Muslims have a fertility rate with each Muslim woman on average giving birth to 3.1 children.¹ Some evidence suggests that restricted maternal nutrition during critical periods of fetal development is associated with permanent alterations to the physiology of the fetus.²⁻⁴ Low birth weight has been shown to affect the morbidity and mortality of the new born and the Marmot Review states that low birth weight in particular is associated with poorer long term health.⁵⁻¹⁰ Other literature has reported that skipping meals during pregnancy can induce physiological stress and is associated with premature birth, suggesting that Ramadan could have adverse effects on fetal development.¹¹⁻¹² Data from the Dutch famine cohort study (1944-1945) however showed that early pregnancy famine exposure was not strongly associated with birth weight or gestational length.¹³ Whilst health agencies advise women that there is medical evidence to show that fasting in pregnancy is not ideal,¹⁴ evidence about possible health consequences is conflicting and there is no definitive guidance.¹⁵⁻²¹ The critical concerns with previous studies are that they have been based on small samples, and/or have not taken account of gestational age when estimating conception date, and/or have not adjusted for important confounders.

Our primary aim was to compare the birth weight of infants born to Muslim mothers who were conceived during Ramadan with their counterparts who had not. Our secondary aim was to explore this question in relation to rates of premature birth. We have focused on time of conception because women would not have been aware they were yet pregnant, therefore highly

likely to have fasted, and because studies have suggested that the effect of fasting on birth weight may be of more concern in the first trimester of pregnancy.²⁰

Methods

Setting and Study Population

The Born in Bradford (BiB) study is a prospective cohort that aims to investigate the impact of environmental, genetic and social factors on health.²² Bradford is located in the North of England and is one of the most deprived cities in the United Kingdom. Bradford District ranks as the 19th most deprived local authority in England (where 1 is the worst deprived local authority and 326 is the least deprived).²³ The infant mortality rate in Bradford is one of the highest in England and Wales (7.0/1000 versus 4.3/1000 live births in 2010-2012). In the most deprived areas of Bradford district the infant mortality rate is substantially higher at 10.2/1000 live births and the risk of dying from congenital anomalies in Bradford is significantly higher in Pakistani babies compared to white babies and also compared to the region or nationally.²⁴ Approximately 20% of Bradford city residents are of South Asian origin. About half of the South Asian population in Bradford are of Mirpuri origin; Mirpur is a predominantly rural district in the province of Azad Kashmir in Pakistan. Bradford has a higher than average birth rate with about half of the babies in the city born to parents of Pakistani origin.

The published protocol for BiB describes in detail the methods of recruitment and outcomes for BiB.²² In summary, a total of 13,776 pregnant women were recruited to the BiB project between March 2007 and December 2010. Women were typically recruited when they attended the Bradford Royal Infirmary (BRI) for a routine oral glucose tolerance test (GTT) at 26-28 weeks gestation. Women who consented to the study at this visit also completed a semi-structured questionnaire that included items about demographic characteristics, lifestyle and health status/history. The methods have been reported here following the STROBE statement.

Definitions and Data Collection

Routinely collected data accessed from maternity records was the source for information on infant birth weight, gestational age, gender of child, parity, diabetes before pregnancy and gestational diabetes. Information on ethnicity, smoking status during pregnancy and educational attainment of the mother were collected from the baseline questionnaire during recruitment (26-28 weeks of pregnancy). Overall, 80% of women who are booked to give birth at BRI attend for their oral GTT. Mothers were asked to self-report their ethnicity (see below). National Health Service (NHS) number was used to link and access routinely collected data. NHS number is a unique identifier for patient medical records allowing excellent data linkage. The 2010 Index of Multiple Deprivation (IMD), a UK government statistic, was used to provide a relative measure of socioeconomic deprivation for area of residence, combining seven domains of deprivation including income, employment, health and disability, education, barriers to housing and services, living environment, and crime into a single deprivation score for each small area in England.²³

All pregnant women who planned to, and then gave birth at the BRI during the period of recruitment were eligible for the BiB project. Twin pregnancies were excluded and assisted conception pregnancies were included. Women who signed the consent form thereby gave consent for their babies to be included in the BiB project at birth. In this study mother-infant pairs were eligible for inclusion if they were Muslim (defined as having reported their religion as Muslim or being of Pakistani or Bangladeshi ethnicity). Data collection in BiB was in three phases and a specific question on religion was not included in phases 1 and 2. However, in phase 3, of those who indicated their ethnicity as Pakistani or Bangladeshi, 91.3% reported their religion as Muslim. In addition, in the 2011 Census 92% of Pakistanis and 90% of Bangladeshi's in the UK reported their religion as Muslim,²⁵ minimising concerns about misclassifications of religion.

Women were considered exposed if they were Muslim and during the years of recruitment to the BiB project a Ramadan period overlapped with their infant conception date, estimated to be 14 days after mothers' last menstrual period (LMP) (date of infant birth minus gestational age in

days). This approach assumes that ovulation and conception typically take place 14 days after the (first day of the) (LMP). Infants were included as exposed if their estimated conception date was in the first 21 days of Ramadan or the seven days prior to Ramadan (meaning they were potentially exposed to maternal fasting in the early weeks following conception). Mother-infant pairs with a conception date in the last seven days of Ramadan (days 22-28) were excluded for two reasons; they would have been exposed to fasting for less than seven days and therefore had minimum exposure and because it can take seven days for an embryo to implant in the uterus, so there will have been less exposure to the environment. Ramadan took place in over the following dates in this study; 2007 (13th September-12 October), 2008 (1 September-30 September), 2009 (22nd August-19 September) and 2010 (11 August–9th September). The period between sunrise and sunset ranged from 10 ³/₄ to 16 hours during the period studied.

Statistical Analyses

Data were analysed in Stata v12 and SAS v9.2. Maternal and child characteristics of the exposed and unexposed groups were compared using two independent sample t-tests, chi-squared tests or fishers exact tests. The association between Ramadan conception and birthweight was carried out using general linear modelling. Unadjusted and adjusted analyses were performed. In the adjusted model, data were adjusted for factors known to be related to birth weight, i.e. maternal smoking status during pregnancy, gestational age, gender of the infant, maternal body mass index (BMI) at booking (continuous variable), nulliparity and gestational diabetes. Since Ramadan is a lunar month and begins about 11 days earlier each year we also adjusted for year of infant birth. The percentages of infants born with low birth weight (<2,500 grams) and percentages of premature births (<37 week gestation) in exposed and unexposed infants were compared using logistic regression analysis. All model assumptions were tested with residual plots and the functional form of the continuous covariates were identified using fractional polynomials. To allow for variation in conception date we also conducted a sensitivity analysis where the conception date was estimated to be 10 days after the date of LMP. The completeness

of the data was assessed; complete case analysis was undertaken with no imputation of missing data.

Sample Size and Power Calculations

It was expected that approximately 6,000 women in the BiB cohort would be Muslim (Pakistani or Bangladeshi). Assuming a twelfth of Muslim babies are conceived during Ramadan the sample would have at least 95% power at the 5% significance level, to detect a difference of 112 grams in birth weight ($sd=665$)²⁶ between those conceived during Ramadan and those conceived during other months of the year. General guidelines suggest at least 10-20 subjects per variable are needed when undertaking regression modelling,²⁷ therefore the sample size is also more than adequate to allow other potential variables of interest/confounders to be included in the modelling process. The sample size would be sufficient to detect a 5% absolute difference in the rate of preterm births between exposed and unexposed women with 92% statistical power.

Results

Characteristics of participants

A total of 5,156 Muslim mother-infant pairs (male infants=51.1%) were eligible for inclusion in the study (9.3% conceived during Ramadan; exposed $n=479$; unexposed $n=4,677$). See Figure 1 for participant flow. The average gestational age of infants was 39.5 weeks with a mean birth weight of 3,137 grams. 9.7% of infants were classified as having low birth weight. On average mothers were 27.9 years old (range=16-49 years) and 95.1% were of Pakistani and 4.9% of Bangladeshi ethnicity. At booking most mothers were recorded as having a healthy BMI (18.5 to 24.9 kg/m^2) (45.5%), with the remainder underweight (5.6% BMI $<18.5 kg/m^2$), overweight (30.1% BMI 25 to 29.9 kg/m^2) or obese (18.9% BMI 30 kg/m^2 or more). 3.3% of mothers smoked during pregnancy and 93.6% lived in the two most deprived quintiles of multiple deprivation. The percentage of maternal missing data was low with BMI being the most incomplete (5% missing). Table 1.

Table 1: Characteristics of cohort (N=5,156)

Characteristics	Exposed N=479	Unexposed N=4,677	Total N=5,156	Missing N (%)
Mother:				
Age (years) mean (sd) n Range	27.9 (5.2) 479 18 to 44	27.9 (5.2) 4677 16 to 49	27.9 (5.2) 5156 16 to 49	0 (0)
Height (metres) mean (sd) n	1.6 (0.06) 469	1.6 (0.06) 4547	1.60 (0.06) 5016	40 (2.5)
Weight (kg) at booking mean (sd) n	66.8 (15.9) 460	64.9 (14.1) 4569 [§]	65.1 (14.3) 5029	127 (2.5)
BMI (kg/m ²) at booking mean (sd) n	26.2 (6.0) 452	25.5 (5.3) 4445	25.6 (5.4) 4897	259 (5.0)
Underweight	20/452 (4.4)	253/4445 (5.7)	273/4897 (5.6)	
Normal	195/452 (43.1)	2031/4445 (45.7)	2226/4897 (45.5)	
Overweight	143/452 (31.6)	1330/4445 (29.9)	1473/4897 (30.1)	
Obese	94/452 (20.8)	831/4445 (18.7)	925/4897 (18.9)	
Ethnicity:				0 (0)
Pakistani	453/479 (94.5)	4450/4677 (95.2)	4903/5156 (95.1)	
Bangladeshi	26/479 (5.4)	227/4677 (4.9)	253/5156 (4.9)	
Education:				79 (1.5)
<5 GCSE equivalent	124/472 (26.3)	1205/4605 (26.2)	1329/5077 (26.2)	
5-GCSE equivalent	156/472 (33.1)	1453/4605 (31.6)	1609/5077 (31.7)	
A-Level equivalent	54/472 (11.4)	607/4605 (13.2)	661/5077 (13.0)	
Higher than A-level	118/472 (25.0)	1198/4605 (26.0)	1316/5077 (25.9)	
Other	20/472 (4.2)	142/4605 (3.1)	162/5077 (3.2)	
Smoking during pregnancy	13/478 (2.7)	158/4664 (3.4)	171/5142 (3.3)	14 (0.3)
Diabetes before pregnancy	2/456 (0.4)	10/4489 (0.2)	12/4945 (0.2)	211(4.1)
Gestational diabetes	43/479 (9.0)	516/4671 (11.1)	559/5150 (10.9)	6 (0.1)
Nulliparous	121/451 (26.8)	1461/4491 (32.5) [§]	1582/4942 (32.0)	214(4.2)
IMD quintile:				1 (0.02)
1 (most deprived)	396/479 (82.7)	3707/4676 (79.3) [§]	4103/5155 (79.6)	
2	48/479 (10.0)	673/4676 (14.4)	721/5155 (14.0)	
3	34/479 (7.1)	262/4676 (5.6)	296/5155 (5.7)	
4	1/479 (0.2)	23/4676 (0.5)	24/5155 (0.5)	
5 (least deprived)	0/479 (0)	11/4676 (0.2)	11/5155 (0.2)	
Year of infant birth				9 (0.2)
2007	115/476 (24.2)	1021/4671 (21.9)	1136/5147 (22.1)	
2008	105/476 (22.1)	1193/4671 (25.5)	1298/5147 (25.2)	
2009	148/476 (31.1)	1320/4671 (28.3)	1468/5147 (28.5)	
2010	108/476 (22.7)	1137/4671 (24.3)	1245/5147 (24.2)	
Infant gender – male	274/479 (57.2)	2358/4677 (50.4) [§]	2632/5156 (51.1)	0 (0)
Gestation (weeks) mean(sd) n	39.5 (1.9) 479	39.4 (1.7) 4677	39.5 (1.7) 5156	(0)
Birth weight (g) mean(sd) n	3179.0 (548.8) 479	3132.9 (519.0) 4677	3137.2 (522.0) 5156	0 (0)
Low birth weight (<2500g)	47/479 (9.8)	410/4677 (8.8)	457/5156 (8.9)	0 (0)
Preterm births (<37 weeks)	25/479 (5.2)	227/4677 (4.9)	252/5156 (4.9)	0 (0)
Subscapular skinfold thickness at birth (mm) mean(sd) n	4.77 (1.29) 291	4.64 (1.07) 3349	4.65 (1.09) 3640	1516 (29.4)
Triceps skinfold thickness at birth (mm) mean(sd) n	5.08 (1.20) 294	5.02 (1.05) 3356	5.02 (1.06) 3650	1506 (29.2)

Figures are n/N (percentage) unless stated otherwise. Exposed=conception occurred during period 7 days prior to Ramadan and 21st day of Ramadan. Conception=14 days after estimated date of last period. Numbers in parenthesis are percentages unless otherwise stated.

[§]significant difference between exposed and unexposed groups (p<0.05). Gestational diabetes defined using the fasting and postload

glucose according to World Health Organisation (WHO) criteria at the time women were pregnant as either a fasting glucose ≥ 6.1 mmol/L or a 2 h postload glucose ≥ 7.8 mmol/L. Standard WHO cut-offs were used to define BMI categories. GCSE's refers to General Certificate of Secondary Education. Five GCSE's relates to standard minimum level of education when leaving school. Information about the intra- and inter-observer technical error of measurement values for skinfold measurement are reported elsewhere.²⁸

Representativeness of the study sample

The study sample represents the overall BiB project cohort (n=13,773) relatively well, particularly in terms of IMD quintile distribution, infant birth weight, gestational age, percentage low birth weight and infant gender.²⁹

Birth weight

After adjusting for confounders there was no significant difference in birth weight between infants conceived during Ramadan (n=425) and those not conceived during Ramadan (n=4252 (adjusted mean difference = 24.3 grams, 95% CI = -16.4 to 64.9). The results remained unchanged in the unadjusted analysis. Sensitivity analysis (adjusting for the same variables) where conception date was assumed to be 10 days after the last menstrual period for defining exposure, did not alter the findings (adjusted mean difference = 22.8 grams, 95% CI -18.5 to 64.1). Results were unchanged in the unadjusted analyses. Tables 2 and 3.

Table 2: Outcomes according to exposure where conception date is assumed to be 14 days after the last menstrual period

Outcomes		Exposed	N	Unexposed	N	Difference
Birth weight (g)	Mean (95% CI)	3179 (3132.2 to 3225.7)	479	3132.9 (3117.9 to 3147.8)	4677	46.1 (-3.0 to 95.2)
	Adjusted mean (95% CI) [#]	3157.5 (3119.0 to 3196.5)	425	3133.5 (3121.3 to 3145.7)	4252	24.3 (-16.4 to 64.9)
		Exposed		Unexposed		Odds ratio (95% CI)
Low birth weight (<2500g)	% (95% CI)	9.8 (7.1 to 12.5)	479	8.8 (8.0 to 9.6)	4677	1.13 (0.82 to 1.56)
	Adjusted % (95% CI) [#]	10.1 (7.5 to 12.6)	425	8.9 (8.2 to 9.6)	4252	1.23 (0.80 to 1.89)
Premature birth (<37	% (95% CI)	5.2 (3.2 to 7.2)	479	4.9 (4.2 to 5.5)	4677	1.08 (0.71 to 1.65)

weeks gestation)						
	Adjusted % (95% CI) [§]	5.4 (3.2 to 7.7)	425	4.9 (4.2 to 5.5)	4252	1.12 (0.71 to 1.77)

[#]adjusted by continuous variables: gestational age (days), BMI, age of mother; categorical variables: gender, smoking status, gestational diabetes, nulliparity; year of birth. [§]adjusted by continuous variables: BMI, age of mother; categorical variables: gender, smoking status, gestational diabetes, nulliparity & year of birth.

Proportion of low birth weight infants

There was no significant difference in the proportion of infants with low birth weight (<2,500 grams) born to exposed (n=47/479; 9.8%) and unexposed women (n=410/4,677: 8.8%) with and without adjustment for confounders. Similar results were found in the sensitivity analyses (exposed n=48/468: 10.3%; unexposed: n=409/4,688: 8.7%). Tables 2 and 3.

Proportion of premature births

The percentage of premature births (<37 weeks gestation) were similar in those who were exposed to Ramadan during conception compared to those unexposed (5.2% vs 4.9%, OR=1.08 (0.71 to 1.65). Adjusting for confounders did not alter the results. Sensitivity analysis generated similar results (exposed n=27/468: 5.8%; unexposed: n=225/4,688: 4.8%). See Tables 2 and 3.

Table 3: Sensitivity analysis: Outcomes according to exposure where conception date is assumed to be 10 days after the last menstrual period

Outcomes		Exposed	N	Unexposed	N	Difference
Birth weight (g)	Mean (95% CI)	3158.0 (3111.2 to 3205.8)	468	3135.0 (3120.1 to 3150)	4688	23.4 (-26.2 to 73.1)
	Adjusted mean (95% CI) [#]	3156.5 (3117.0 to 3195.9)	411	3133.7 (3121.5 to 3145.8)	4266	22.8 (-18.5 to 64.1)
		Exposed		Unexposed		Odds ratio (95% CI)
Low birth weight (<2500g)	% (95% CI)	10.3 (7.5 to 13.0)	468	8.7 (7.9 to 9.5)	4688	1.20 (0.87 to 1.64)
	Adjusted % (95% CI) [#]	9.6 (7.1 to 12.1)	411	8.9 (8.2 to 9.6)	4266	1.12 (0.72 to 1.75)
Premature birth (<37 weeks gestation)	% (95% CI)	5.8 (3.7 to 7.9)	468	4.8 (4.2 to 5.4)	4688	1.21 (0.81 to 1.83)
	Adjusted % (95% CI) [§]	5.8 (3.5 to 8.1)	411	4.8 (4.2 to 5.5)	4266	1.21 (0.78 to 1.89)

[#]adjusted by continuous variables: gestational age (days), BMI, age of mother; categorical variables: gender, smoking status, gestational diabetes, nulliparity; year of birth. [§]adjusted by continuous variables: BMI, age of mother; categorical variables: gender, smoking status, gestational diabetes, nulliparity & year of birth.

DISCUSSION

Main findings

Muslim women planning to conceive a child will often ask their doctor or healthcare provider whether it is safe to fast during Ramadan but evidence on this question has been inconsistent. After adjustment for confounders Muslim infants conceived during Ramadan were not born smaller and had a similar risk of premature birth to children conceived at other times of the year. These findings remained unchanged in the sensitivity analyses.

Interpretation

The evidence on whether fasting during Ramadan in early pregnancy has a detrimental effect on birth weight is contradictory. Several studies have reported that infants estimated to have been conceived during Ramadan are born smaller than babies conceived outside of Ramadan.¹⁹⁻²⁰ Previous studies however have typically included small numbers of exposed women and/or not accounted for important confounders likely to influence birth weight (e.g. gestational age & smoking). The two largest studies^{15,17} however have reported no association between fasting in early pregnancy and infant birth weight, although both studies have methodological concerns that would have been likely to introduce bias. Cross¹⁷ compared birth weights of 13,351 babies born between 1964-1984 with two age matched comparator groups; white (n=13,351) and non-Muslim Asians (n=5,106) and Alwasel¹⁵ compared the birth weight of 1,598 cases who had been exposed to Ramadan in early pregnancy with 1,822 unexposed cases. Both studies only included infants who were born at 'term', defined as at least 37 or 38 weeks gestation.^{15,17} If maternal fasting during Ramadan induced premature birth and/or low birth weight, these studies will have discounted or underestimated these effects if such associations existed. Cross and colleagues categorised infants as Muslim according to the first three letters of the mother's surname and not using any factual information about religious or ethnic status. Additionally, Cross compared birthweights of participants across groups of Muslims and non-

Muslims, rather than Muslims who were and were not in utero during Ramadan. A study by van Ewijk²¹ which investigated the associations between prenatal exposure to Ramadan across trimesters with stature and thinness in adulthood has some relevance here (included n=1,237 Muslims conceived during Ramadan; n=1,520 not in utero during Ramadan). A measure of birth weight was not included in this study, but the authors reported that adult Muslims who were conceived during Ramadan had a lower BMI than Muslims not conceived during Ramadan (BMI difference = -0.37 kg/m², 95% CI: -0.71 to -0.03). Given the van Ewijk study²¹ is reporting associations from birth to adulthood over two-three decades, it is possible that other lifestyle or environmental factors are responsible for the observed difference. The van Ewijk study did not take into account gestational age at birth either, which may have led to some misclassification of exposure.

Premature birth is one of the leading causes of neonatal morbidity. Our results for premature birth are consistent with previous smaller studies (which are typically involve less than ~300 participants), which have reported that Ramadan fasting was not associated with higher rates of premature birth and/or gestational age at birth.^{16, 30}

Strengths and weaknesses

This study was epidemiological in nature and therefore we do not know for certain the extent to which women fasted or the degree of religious observance, although evidence has shown that most Muslims observe fasting during Ramadan¹ As conception would have just taken place the vast majority of exposed women will not have known yet that they were pregnant therefore very likely to have fasted. Moreover, it would be unlikely that a RCT on this question would take place therefore this study provides the best available evidence on which to base advice to the public. Children defined as not exposed to Ramadan fasting during conception may have been exposed in utero later in pregnancy; as other studies have done,^{19,21} we could have further subdivided the sample according to the trimester during pregnancy that Ramadan occurred. We did not take this approach because as pregnancy progresses it becomes increasing

uncertain and unlikely that mothers will have fasted¹⁶ and exposure classification will not have been robust. Another approach we might have taken would have been to compare non-Muslim children from other ethnic groups (e.g. White British) with exposed Muslim women. This approach however fails to consider that the cultural and environmental conditions of these groups (e.g. diet of mothers, family environment etc.) will have been different. Some misclassification of exposure may have occurred because of differing degrees of religious observance and adherence to practices during Ramadan between participants (natural variation of observance in any religion).

Date of conception (14 days after LMP) was calculated using date of birth minus gestational age and may be subject to some small misclassifications of exposure, although in the sensitivity analysis where we varied date of conception made no difference to the results. The BiB cohort study recruited women around 26-28 weeks gestation which could mean we have not included very early preterm deliveries, although the vast majority of preterm deliveries will have occurred later than 28 weeks gestation. South Asian Muslim populations living in the UK tend to have a higher total fertility rate than other ethnic and/or religious groups (i.e. shorter inter-pregnancy interval),¹ which may have influenced the results, but this data is not available within the BiB cohort dataset. This study took place in England and may not be directly relevant to other countries with different environmental conditions (e.g. day length, ambient temperature, humidity). Data on exposures such as altered sleep patterns, acute and/or chronic hypohydration, altered mood, and changes to other lifestyle behaviours was not collected but this information may have aided our interpretations of the findings.

There are several strengths to our study. It includes data from a large contemporary sample of South Asian Muslim women and is based on naturally occurring data. The month at which a baby is conceived occurs mostly at random. It is not affected by social class, parent's age or their health status. Therefore observing patterns according to month of conception is a powerful study design to identify influences of the environment before birth. The physical health

and socioeconomic characteristics of exposed and unexposed women were generally similar. To our knowledge this is the largest study to have included neonatal birth weight and taken into account gestational age when estimating date of conception, as well including gestational age as a covariate in the analyses. This is an important strength of our study for two critical reasons; gestational age directly influences birth weight and information on gestational age allows us to more accurately classify exposure than previous studies. We were also able to adjust for other health and lifestyle variables which other studies have not done (e.g. gestational diabetes, parity & early pregnancy maternal BMI) which is critical for reducing confounding. The level of missing data was low and the maternal characteristics of those cases with missing data were not significantly different to those with complete data therefore we consider robust conclusions can be made from our complete case analysis. BiB infants were born between 2007-2010; Ramadan during these years took place in August and September where the number of hours between sunrise and sunset spans the longest of any season (i.e. summer) of the calendar year. In the summer season Ramadan fasting in Northern Europe lasts between 11-16 hours per day, whereas in winter it lasts for approximately 6-7 hours per day. Our study therefore presents data where mothers experienced a substantially lengthy period of exposure to Ramadan fasting each day during Ramadan. Our analyses include adjustment for year of birth to allow for the potential effect of day length and climactic conditions. Most studies to date have focused on birth weight and there is a lack of evidence about other important clinical outcomes such as preterm birth.

In conclusion, we found no evidence that maternal fasting during Ramadan is associated with increased risk of infants being born smaller or sooner than infants not conceived during Ramadan. As part of preconception care, healthy Muslim women and their partners can be advised Ramadan fasting is unlikely to have a detrimental effect on the size of their infant at birth and appears not to increase the probability of premature birth. Future prospective studies specifically designed to collect maternal data on lifestyle behaviours during Ramadan are needed to provide a definitive answer on the relationship between Ramadan exposure and maternal and

fetal outcomes. These findings are important to the 230 million Muslim women around the world who are of reproductive age and the 713 million babies who they give birth to during their lifetime.

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Contributions

AD conceived the original idea for the study. AD wrote the protocol with contributions from MP, KJ, PA, SC, AR and MB. AR advised on statistical methodology and conducted all the analyses. AD drafted the article and all other authors commented on this draft. AD is the guarantor.

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Abbreviations: BMI: Body mass index, OR: odds ratio, BiB: Born in Bradford, GTT: glucose tolerance test,

Ethical approval

Ethical approval for the BIB project was granted by the Bradford Research Ethics Committee (Ref: 07/H1302/112).

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Data sharing

No additional data are available

References

1. The World's Muslims: Unity and Diversity. Pew Research Center. The Pew Forum on Religion and Public Life. 2012. www.pewforum.org/files/2012/08/the-worlds-muslims-full-report.pdf. Date accessed 21st October 2015.
2. Malhotra A, Scott PH, Scott J., et al. Metabolic changes in Asian Muslim pregnant mothers observing the Ramadan fast in Britain. *Br J Nutr* 1989; 61:663-672.
3. Prentice AM, Prentice A, Lamb WH., et al. Metabolic consequences of fasting during Ramadan in pregnant and lactating women. *Hum Nutr Clin Nutr* 1983;37:282-294.
4. Khoshdel A, Kheiri S , Nasiri J., et al. The effect of Ramadan fasting on serum leptin, neuropeptide Y and insulin in pregnant women. *Med J Islamic Republic of Iran* 2014;14:28:92.
5. Barker DJP, Winter PD, Osmond C, Margetts B, Simmonds SJ. Weight in infancy and death from ischaemic heart disease. *Lancet* 1989;2:577-80.
6. Marmot, M. Fair Society, Healthy Lives—Strategic Review of Health Inequalities in England post. London: The Marmot Review. 2010.
7. Harding JE. The nutritional basis of the fetal origins of adult disease. *I J Epidemiol* 2001;30:15-23.
8. Roseboom T, de Rooij S, Painter R. The Dutch famine and its long-term consequences for adult health. *Early Human Development* 2006;82:485-491.
9. Hack M, Flannery DJ, Schluchter M, Carter L, Borawski E, Klein N. Outcomes in young adulthood for very low-birth weight infants. *NEJM* 2002;345:149-152.
10. Osmond C, Barker DJP. Fetal, infant and childhood growth are predictors of coronary heart disease, diabetes and hypertension in adult men and women. *Environ Health Persp* 2000;108:545-553.
11. Siega-Riz AM, Herrmann TS, Savitz DA, Thorp JM. Frequency of eating during pregnancy and its effect on preterm delivery. *Amer J Epidemiol* 2001;153:647-652.
12. Herrmann TS, Siega-Riz AM, Hobel CJ, Aurora C, Dunkel-Schetter C. Prolonged periods without food intake during pregnancy increase risk for elevated maternal corticotropin-releasing hormone concentrations. *Am J Obstet Gynecol Obstetrics* 2001;186:403-412.
13. Stein Z, Susser M. The Dutch Famine, 1944-1945, and the reproductive process. I. Effects on Six Indices at Birth. *Pediat. Res* 1975;9:70-76.

14. NHS choices. Healthy Ramadan.
www.nhs.uk/livewell/healthynamadan/Pages/healthynamadanhome.aspx. Date accessed 21st October 2015.
15. Alswasl SH, Abotalib Z, Aljarallah JS, et al. Changes in placenta size during Ramadan. *Placenta* 2010;31:607-610.
16. Petherick ES, Tuffnell D, Wright J. Experiences and outcomes of maternal Ramadan fasting during pregnancy: results from a sub-cohort of the Born in Bradford birth cohort study. *BMC Pregnancy and Childbirth* 2014;14:335.
17. Cross JH, Eminson J, Wharton BA. Ramadan and birth weight at full term in Asian Moslem pregnant women in Birmingham. *Arch Dis Childhood* 1990; 65; 1053-1056.
18. Sakar MN, Gultekin H, Demir B., et al. Ramadan fasting and pregnancy: implications for fetal development in summer season. *J Perinatal Medicine* 2015;43:319-23.
19. Alsawel SH, Harrath A, Aljarallah JS, et al. Intergenerational effects of in utero exposure to Ramadan in Tunisia. *Amer J Hum Biol* 2013; 25:341-343.
20. Savitri |AI, Yadegari N, Bakker J, et al. Ramadan fasting and newborn's birth weight in pregnant Muslim women in The Netherlands. *Br J Nutrition* 2014;112:1503-1509.
21. van Ewijk RG, Painter RC, Roseboom TJ. Associations of prenatal exposure to Ramadan with small stature and thinness in adulthood: results from a large Indonesian population-based study. *Amer J Epidemiol* 2013;177:729-736.
22. Born in Bradford Collaborative Group. Born in Bradford, a cohort study of babies born in Bradford and their parents: protocol for recruitment phase. *BMC Public Health* 2008; 8:327 doi:10.1186/1471-2458-8-327.
23. The English Indices of Multiple Deprivation. Department of Communities and Local Government. <https://www.gov.uk/government/statistics/english-indices-of-deprivation-2010>. Date Accessed 12th February 2015.
24. Data atlas for infant mortality in England and Wales
<http://www.chimat.org.uk/default.aspx?QN=CHMT1>. Date accessed 12 January 2016.
25. Office for National Statistics. Datablog: UK Census: religion by age, ethnicity and country of birth. *The Guardian*. 16 May 2013. Retrieved 5 July 2014.
26. Kelly Y, Panico L, Bartley M., et al Why does birthweight vary among ethnic groups in the UK? Findings from the Millennium Cohort Study. *J Public Health* 2009;31:131-7.
27. Harrell F. Regression modeling strategies with applications to linear models, logistic regression and survival analysis. New York: Springer-Verlag,2001.

28. Westa J, Manchesterb B, Wright J, Lawlor D, Waiblinger D. Reliability of routine clinical measurements of neonatal circumferences and research measurements of neonatal skinfold thicknesses: findings from the Born in Bradford study. *Paed Perinatal Epidemiol* 2011; 25:164-171.
29. Wright J, Small N, Raynor P et al. Cohort profile: the born in Bradford multi-ethnic family cohort study. *I J of Epidemiol* 2013;42;978-991.
30. Hizli D, Yilmaz SS, Onaran Y, Kafali H, Danişman N, Mollamahmutoğlu L. Impact of maternal fasting during Ramadan on fetal Doppler parameters, maternal lipid levels and neonatal outcomes. *J Matern Fetal Neonatal Med.* 2012 ;25:975-977.