

Original Contribution

Associations of Prenatal Exposure to Ramadan with Small Stature and Thinness in Adulthood: Results From a Large Indonesian Population-Based Study

Reyn J. G. van Ewijk*, Rebecca C. Painter, and Tessa J. Roseboom

* Correspondence to Dr. Reyn van Ewijk, Institute of Medical Biostatistics, Epidemiology, and Informatics, University Medical Center Mainz, Langenbeckstrasse 1, 55101 Mainz, Germany (e-mail: vanewijk@imbei.uni-mainz.de).

Initially submitted February 21, 2012; accepted for publication August 16, 2012.

A growing body of evidence suggests that maternal diet during pregnancy can lead to permanent alterations to the physiology of the fetus. It is unknown whether intermittent maternal fasting during Ramadan has long-term associations with the offspring's body composition. By using data from the third wave of the Indonesian Family Life Survey (2000), we compared the body mass indices (weight (kg)/height (m)²) of Muslims who had been in utero during Ramadan with those of Muslims who had not been in utero during Ramadan. Adult Muslims who had been in utero during Ramadan were slightly thinner than Muslims who had not been in utero during Ramadan (adjusted adult body mass index: -0.32 , 95% confidence interval: -0.57 , -0.06). Those who were conceived during Ramadan also had smaller stature, being on average 0.80 cm shorter than those who were not exposed to Ramadan prenatally. Among non-Muslims, no such associations were found. This study suggests that exposure to Ramadan during pregnancy may have lasting consequences for adult body size of the offspring.

anthropometry; lifestyle; pregnancy; prenatal; nutrition; Ramadan fasting

Abbreviations: BMI, body mass index; CI, confidence interval.

Editor's note: An invited commentary on this article appears on page 737, and the authors' response appears on page 741.

A growing body of evidence suggests that maternal diet during pregnancy can permanently program the fetus and thereby affect its later health (1, 2). Previous studies of drastically reduced nutritional intake during pregnancy have reported both increases (mainly among women) and decreases in adult offspring's body mass index (BMI, measured as weight (kg)/height (m)²) (3–11). It is unknown whether intermittent maternal fasting during Ramadan has long-term effects on the offspring's body composition. Ramadan is the ninth month of the Islamic lunar calendar, and fasting during Ramadan is a religious obligation for healthy Muslim adults. When observing Ramadan, people consume no food or drink (including water) from dawn to sunset. They often reduce their levels of activity during the day and are more active at night. Studies have shown that body weight tends to decrease during Ramadan in both men

and women (12, 13). It has been suggested that this is mainly an effect of decreased fluid intake (14–16), although reduced caloric intake has also been reported, particularly among pregnant women (17). Although pregnant women are allowed to defer fasting until after pregnancy, many pregnant women prefer to share the spiritual and social experiences of Ramadan with their families, or they want to avoid having to make up for the fast after pregnancy, as religious rules prescribe. Around 70%–90% of Muslim women around the world, including those in Singapore, Iran, the United Kingdom, and West Africa, report fasting during pregnancy (18–21).

Pregnant women who fast during Ramadan have been shown to have symptoms of accelerated starvation, which is characterized by low serum levels of glucose and alanine and especially high levels of free fatty acids (20, 21). Depending on its timing during gestation, Ramadan fasting has been shown to be associated with the size of the baby and the placenta at birth (21–23). Almond and Mazumder (22) and Van Ewijk (24) showed that prenatal exposure to Ramadan is associated with health problems later in life.

This study investigates the association of Ramadan exposure during pregnancy with adult offspring anthropometry. We used data from Indonesia, a country with 2 important advantages to those studying this topic. First, it is the country with the largest Muslim population in the world: 86% of its 246 million citizens are Muslims (25). Second, Indonesia's location on the equator means that daylight times, and thus fasting times during Ramadan, are about the same each year (about 13.5 hours), irrespective of the Gregorian month in which Ramadan falls.

MATERIALS AND METHODS

Indonesian Family Life Survey

The Indonesian Family Life Survey is a longitudinal survey carried out by the RAND Corporation (Santa Monica, California) that collects information on a large set of health, economic, and social indicators. The third wave of the survey was carried out in 2000. Sampling took place at the household level. The sample is representative of the population of 13 of the (then) 26 Indonesian provinces, which represent 83% of the total Indonesian population. The excluded provinces were mainly peripherally located and less densely populated. The total sample size was 43,649 persons in 10,435 households. A more detailed description of sampling procedures and response rates is given elsewhere (26). In Indonesia, as in many developing countries, some people do not know their exact dates of birth. This was true for 31% of our sample who had to be excluded. Excluding persons who were under 18 years of age further reduced the sample size to 16,873. Of these, anthropometric measures were taken for 15,483, of whom 88% were self-reported Muslims. We excluded 470 non-Muslims from Bali, where only 15% of the population is Muslim. All other non-Muslims lived in provinces where the majority of the population is Muslim. Non-Muslims form a good comparison group because they experience the same circumstances

during Ramadan as do Muslims (e.g., natural catastrophes coinciding with Ramadan, general changes in lifestyle, holidays) except for the actual observance of Ramadan.

Outcome measures

Height and weight were measured by trained nurses. In adults, height was measured in a standing position to the nearest millimeter by using Shorr measuring boards (Weigh and Measure, LLC, Olney, Maryland). Weight was measured by using portable digital floor-model scales (SECA GmbH and Co., Hamburg, Germany), which were accurate to the nearest 0.1 kg and which were recalibrated approximately once a week. Participants wore light clothing and no shoes during measurement. Health teams revisited all sampled areas affected by broken scales to remeasure participants (26).

Ramadan exposure

We assigned subjects to categories of prenatal exposure to Ramadan on the basis of religion and date of birth (Figure 1). Subjects were considered to have been exposed to Ramadan in utero if they indicated they were Muslim and a Ramadan overlapped with the period of 266 days before their dates of birth (27). The reference group consisted of Muslims who were not in utero during Ramadan (i.e., those who were conceived within a relatively narrow time frame of about 60 days per Islamic year beginning immediately after a period of Ramadan and ending 266 days before the next Ramadan).

We excluded data from 893 persons who we calculated as having been conceived <21 days after the end of a Ramadan (calculated as birth date minus 266 days) because, if they were born postterm, their classification as "unexposed" might be incorrect, which would create undue measurement error.

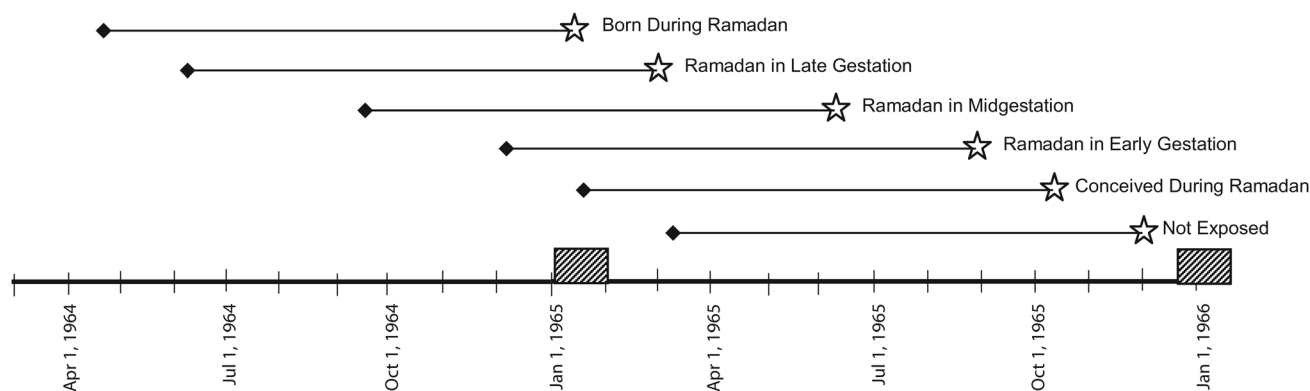


Figure 1. Calculating the overlap of Ramadan and gestation by using birth dates, the Indonesian Family Life Survey, Wave 3, in 2000. The figure shows how in utero exposure to Ramadan was determined for persons born in 1965 (year chosen for example purposes). Ramadans (indicated by shaded areas) took place from January 3 to February 1, 1965, and from December 23, 1965, to January 21, 1966. Stars indicate birth dates as reported by participants. Diamonds indicate the calculated date of conception. Horizontal lines indicate the calculated period of gestation (266 days). Apr, April; Jan, January; Jul, July; Oct, October.

To examine differential associations according to the timing of Ramadan during gestation, we divided those exposed to Ramadan into 5 subgroups. The first 2 subgroups consisted of those who were conceived during Ramadan and those who were born during Ramadan. The other 3 subgroups consisted of those who experienced an entire Ramadan in utero but who were not born during Ramadan. These groups were defined as those for whom Ramadan began during the first trimester of pregnancy (days 1–89 of gestation), the second trimester of pregnancy (days 90–178 of gestation), and the third trimester of pregnancy (days 179–266 of gestation).

Statistical methods

We compared data on the BMI, weight, and height of Muslims who were exposed to Ramadan in utero with those of Muslims who were not exposed to Ramadan in utero. Subsequently, we investigated whether associations differed according to the period of gestation during which Ramadan fell, and whether associations differed between men and women. We also investigated whether similar trends were present among non-Muslims to determine whether the associations may be caused by changes associated with the observance of Ramadan itself or by other factors coinciding with Ramadan.

For all analyses, we performed ordinary least squares regressions that adjust for sex, age (in days) when measurements were taken, age squared, month of birth (as a categorical variable), and family fixed effects. The Islamic calendar is a lunar calendar, and years are somewhat shorter than in the commonly used Gregorian calendar. Depending on moon sightings, Ramadan starts about 11 days earlier each year. We used this “shifting over the year” to separate the effects of Ramadan from season-of-birth effects by including month-of-birth dummy variables as covariates in our regressions. Standard errors were adjusted for clustering of the data at the family level. The inclusion of family fixed effects means that statistical identification comes only from within-family comparisons; that is, systematic between-family differences (e.g., those arising because of shared nutritional patterns) are filtered out (28). Subjects in our sample came from families comprising an average of 2.5 people aged 18 years or older. Outliers on the dependent variables (weight, height, and BMI) were truncated at 5 standard deviations from the mean. This affected <0.1% of the cases, and the results were robust to taking other cutoffs for the truncation, to removing these cases entirely, and to using the untruncated values. Note that in our regressions we did not adjust for covariates such as birth weight and health because these may themselves be dependent on prenatal Ramadan exposure; therefore, including such covariates could potentially bias our results (22, 24).

We estimated 2 alternative models as a sensitivity check. It is essential to thoroughly control for age because weight and BMI may change in nonlinear ways over the life course. Our main analyses controlled for age and age squared, and we additionally estimated regressions in which we included dummy variables for age (measured in years) to filter out as much age-induced variation in BMI, weight, and height as possible. We also estimated regressions in which the family

fixed effects were replaced by random effects. Fixed effects models have an advantage over random effects models in that they remove any between-family differences (both measured and unmeasured) from the data; however, they have the disadvantage that only families consisting of multiple people who are discordant on the exposure variable contribute to the identification.

Importantly, we classified Muslim subjects on the basis of whether and when Ramadan occurred while they were in utero, but we lacked information about whether their mothers had actually fasted. Instead, we made the implicit assumption that all Muslim women who were pregnant during Ramadan did fast. This intention-to-treat approach underestimates the true associations of Ramadan fasting during pregnancy, and our results could hence be regarded as a lower bound of the association.

RESULTS

Baseline characteristics

A total of 14,120 people (12,900 Muslims and 1,220 non-Muslims) had measurements of height and weight and information on date of birth and religion and were thus available for the analyses. The mean age of all participants was 34.6 (range: 18.0–98.6) years. The mean height was 162.4 cm for men and 150.9 cm for women. Non-Muslims were slightly older, heavier, and taller, as well as more likely than Muslims to be overweight and to have completed high school. They also were more likely to live in urban areas (Table 1).

Ramadan exposure

Adult Muslims who had been exposed to Ramadan in utero were slightly thinner than Muslims who had not been exposed. The average adult BMI of Muslims who were exposed to Ramadan in utero was 0.32 units lower (BMI difference: -0.32 , 95% confidence interval (CI): -0.57 , -0.06) after adjustment for the covariates. This was mainly due to a reduction in weight of -0.85 (95% CI: -1.54 , -0.17) kg among exposed Muslims. Muslims who were exposed to Ramadan during gestation were 0.20 cm shorter than those who were not exposed, but this difference was not statistically significant (95% CI: -0.59 , 0.19).

Timing of exposure to Ramadan

Both Muslims who were conceived during Ramadan and Muslims who had been in utero during Ramadan in mid- or late gestation had lower BMIs than otherwise comparable unexposed Muslims. The average adult BMI of Muslims who were conceived during Ramadan was 0.37 units lower (BMI difference = -0.37 , 95% CI: -0.71 , -0.03) than that of Muslims who were not exposed to Ramadan in utero. For those who were exposed to Ramadan in midgestation, this difference was 0.42 units (BMI difference = -0.42 , 95% CI: -0.72 , -0.13), and for those who were exposed in late gestation, the difference was 0.43 units (BMI difference = -0.43 , 95% CI: -0.74 , -0.12). This was mainly due to associations

Table 1. Characteristics of Muslims and Non-Muslims Aged 18 Years or Older in the Indonesian Family Life Survey, Wave 3, in 2000

	Muslims			Non-Muslims		
	Mean (SD)	No. ^a	No. ^b	Mean (SD)	No. ^a	No. ^b
Age, years	34.31 (13.05)		12,900	37.99 (14.95)		1,220
Male sex, %	50 (50)	6,494	12,900	49 (50)	595	1,220
BMI ^c	21.87 (3.66)		12,856	22.67 (3.9)		1,212
Weight, kg	53.63 (9.88)		12,861	56.28 (10.9)		1,213
Height, cm	156.56 (8.14)		12,895	157.53 (8.5)		1,219
BMI category ^d						
Overweight, %	18 (38)	2,281	12,856	25 (43)	300	1,212
Obese, %	3 (18)	413	12,856	4 (20)	50	1,212
Underweight, %	15 (36)	1,986	12,856	12 (32)	145	1,212
Completed senior high school, %	37 (48)	4,747	12,848	51 (50)	618	1,215
Lives in urban area, %	58 (49)	7,435	12,900	71 (46)	863	1,220
Exposure to Ramadan						
Not in utero during Ramadan, %	12 (32)	1,520	12,900	12 (32)	143	1,220
In utero during Ramadan, %	88 (32)	11,380	12,900	88 (32)	1,077	1,220
Conceived during Ramadan, %	10 (29)	1,237	12,900	9 (29)	110	1,220
Ramadan in early gestation, %	28 (45)	3,598	12,900	25 (44)	311	1,220
Ramadan in midgestation, %	25 (44)	3,273	12,900	28 (45)	336	1,220
Ramadan in late gestation, %	17 (38)	2,196	12,900	18 (38)	220	1,220
Born during Ramadan, %	8 (28)	1,076	12,900	8 (27)	100	1,220

Abbreviations: BMI, body mass index; SD, standard deviation.

^a Number of participants with the characteristic (for binary variables).

^b Number of participants for whom data were available.

^c BMI is calculated as weight (kg)/height (m)².

^d BMI categories were defined as follows: overweight, BMI ≥ 25 – <30 ; obese, BMI ≥ 30 ; underweight, BMI ≤ 18.5 .

with weight but not with height (Table 2). Muslims who were conceived during Ramadan also had reduced height; they were, on average, 0.80 cm shorter than those who were

not exposed to Ramadan in utero (height difference -0.80 cm, 95% CI: -1.33 , -0.26). The associations were similar for men and women.

Table 2. Associations Between Having Been in Utero During Ramadan With Weight, Height, and BMI in Muslims Aged ≥ 18 Years, Indonesian Family Life Survey, Wave 3, in 2000^a

Exposure to Ramadan	BMI ^b (n = 12,856)		Weight, kg (n = 12,861)		Height, cm (n = 12,895)	
	β^c	95% CI	β^c	95% CI	β^c	95% CI
Not in utero during Ramadan	0.00	Referent	0.00	Referent	0.00	Referent
In utero during Ramadan	-0.32^*	-0.57 , -0.06	-0.85^*	-1.54 , -0.17	-0.20	-0.59 , 0.19
Conceived during Ramadan	-0.37^*	-0.71 , -0.03	-1.42^{**}	-2.32 , -0.53	-0.80^{**}	-1.33 , -0.26
Ramadan in early gestation	-0.24	-0.53 , 0.04	-0.64	-1.41 , 0.13	-0.12	-0.56 , 0.32
Ramadan in midgestation	-0.42^{**}	-0.72 , -0.13	-0.93^*	-1.72 , -0.14	-0.01	-0.46 , 0.44
Ramadan in late gestation	-0.43^{**}	-0.74 , -0.12	-1.06^*	-1.88 , -0.25	-0.12	-0.58 , 0.35
Born during Ramadan	-0.04	-0.40 , 0.32	-0.32	-1.28 , 0.64	-0.37	-0.93 , 0.20

Abbreviations: BMI, body mass index; CI, confidence interval.

* $P < 0.05$; ** $P < 0.01$.

^a Results from 2 separate linear regressions per outcome that adjust for age (measured in days), age squared, sex, month of birth, and family fixed effects. Data represent 6,697 Muslim families.

^b BMI is calculated as weight (kg)/height (m)².

^c β , unstandardized regression coefficient.

Table 3. Associations^a Between Having Been in Utero During Ramadan With Weight, Height, and BMI in Non-Muslims Aged ≥ 18 Years, Indonesian Family Life Survey, Wave 3, in 2000^b

Exposure to Ramadan	BMI ^c (n = 1,212)		Weight, kg (n = 1,213)		Height, cm (n = 1,219)	
	β^d	95% CI	β^d	95% CI	β^d	95% CI
Not in utero during Ramadan	0.00	Referent	0.00	Referent	0.00	Referent
In utero during Ramadan	0.08	-0.77, 0.93	0.07	-2.25, 2.40	-0.07	-1.27, 1.13
Conceived during Ramadan	-0.21	-1.43, 1.01	-1.12	-4.34, 2.10	-0.44	-2.08, 1.21
Ramadan in early gestation	0.38	-0.52, 1.27	0.78	-1.69, 3.26	-0.19	-1.55, 1.17
Ramadan in midgestation	0.73	-0.22, 1.68	2.13	-0.40, 4.67	0.50	-0.85, 1.86
Ramadan in late gestation	-0.67	-1.70, 0.35	-1.93	-4.77, 0.90	-0.18	-1.62, 1.25
Born during Ramadan	-0.81	-2.20, 0.58	-2.99	-6.77, 0.79	-1.20	-3.09, 0.69

Abbreviations: BMI, body mass index; CI, confidence interval.

^a No significant associations were found, with significance defined as $P < 0.05$.

^b Results from 2 separate linear regressions per outcome that adjust for age (measured in days), age squared, sex, month of birth, and family fixed effects. Data represent 640 non-Muslim families.

^c BMI is calculated as weight (kg)/height (m)².

^d β , unstandardized regression coefficient.

Non-Muslims

There were no associations between having been in utero during Ramadan and adult BMI, weight, or height among non-Muslims (Table 3). Non-Muslims whose gestations overlapped with Ramadan had BMIs that were, on average, 0.08 units higher (95% CI: -0.77, 0.93) than those of other non-Muslims. Considering the periods of gestation, no similar pattern of associations as for Muslims was observed. All coefficients were nonsignificant, and point estimates went in both directions.

Alternative specifications

The regressions in which age groups (in years) were included yielded estimates that were very similar to those from our main analyses, demonstrating that the results are robust to thoroughly filtering out age-related variation on the dependent variables. In alternative regressions, we replaced the family fixed effects with random effects. The pattern of results was the same as in the fixed effects regressions, although parameter estimates tended to be slightly smaller, which was probably due to strong within-family correlations of variables such as nutrition, anthropometric measures, genetic factors, and lifestyle habits. The confidence intervals for all parameter estimates overlap.

DISCUSSION

This is the first study investigating the association of prenatal exposure to Ramadan with body size in later life. Our findings show that adult Muslims who experienced Ramadan in late- and midgestation were slightly thinner, and those who were conceived during Ramadan were both thinner and shorter.

A recent study in Saudi Arabia showed that Ramadan exposure in mid- or late pregnancy was associated with a reduction in placental size. This implies that Ramadan

exposure influences placental growth once the maternal blood supply is established and maternal blood enters the placenta (23). The authors suggested that such changes in placental size can lead to fetal programming and can therefore have long-term implications for the health of the next generation. Correspondingly, one study showed that prenatal exposure to Ramadan reduced birth weights (22), although the Saudi Arabian study itself failed to replicate this result. Furthermore, previous studies on long-term associations of maternal Ramadan fasting during gestation demonstrated poorer general health, higher pulse pressures, and increased incidence of symptoms indicative of coronary heart problems and type 2 diabetes among adult offspring in Indonesia (24), as well as increased incidence of vision and hearing problems and cognitive disability among adults in Uganda and Iraq (22).

We cannot be sure whether the long-term associations we found are caused by fasting or by other lifestyle factors associated with Ramadan. During Ramadan, fasting pregnant women may have slightly decreased caloric intake and gestational weight gain (17, 29). Studies of babies born around the time of the Dutch famine of 1944–1945 showed that drastically reduced maternal nutritional intake at any stage of gestation was associated with more obesity among female offspring. For male offspring, similar associations were found only among subjects aged 19 years who had been exposed during midgestation, whereas no such associations were found at later ages. No significant associations with height were found (3–6). Recent studies on the 1959–1961 famine following the Chinese Great Leap Forward found that those who were exposed to famine prenatally had lower BMIs in later life (8, 9). These associations were found only in subjects residing in rural areas where the famine was most severe, and some studies have failed to replicate this finding (7–11). Because the Chinese famine lasted several years, studies on this famine were generally not able to pinpoint effect estimates to specific periods of gestation. In contrast to caloric intake during famine, caloric intake during Ramadan

fasting is generally not considered to be drastically reduced; however, Ramadan fasting during pregnancy has been reported to produce metabolic effects similar to those of starvation (20, 21). The difference between our findings and the findings from the Dutch famine might be caused by differences between Indonesia and postfamine Netherlands in food availability throughout the life course. Conditions in Indonesia, where obesity is less of an issue than underweight, are more comparable in that sense to conditions in China in the decades after the famine, exposure to which also led to lower BMIs in later life. Alternatively, the association of prenatal exposure to Ramadan with anthropometric measures in later life may not be the result of starvation-like metabolic effects. Rather, Ramadan may interfere with nocturnal sleep, particularly for those preparing food for the family, because breakfast must be finished before fasting starts, at around 4:30 AM in Indonesia. Not drinking during the daytime may lead to dehydration, and the common practice of consuming sweet food and drinks in the evening might lead to blood glucose surges. All of these might potentially have effects on anthropometric measures in later life. Also, the Ramadan fast may function as a stressor on the fetus. Previous research showed that not eating or drinking for periods exceeding 13 hours induced stress responses in pregnant mothers (30).

We speculate that our finding of thinness and small stature among men and women who had been exposed to Ramadan in utero may be consistent with persistent stunting and wasting. Stunting is a process of decreased growth in infancy and childhood, resulting in smaller stature in later life. Per the United Nations Children's Fund definition, which we use here, "wasting" refers to a weight-for-height that is considerably below standard. Both are highly prevalent in Indonesia and have been so historically, especially among the cohorts studied here (31). Stunting and wasting are both associated with morbidity and mortality and correlate strongly with prenatal conditions (32). In developing countries, stunting is very hard to reverse by improved nutrition and subsequent catch-up growth after the first few years of life (33, 34). The current study does not have access to data on birth weight and early childhood growth, so future longitudinal research will need to assess this hypothesis. Alternatively, lower attained height and weight may be secondary to an increased susceptibility to illness.

There are a few limitations to our study. First, our estimates are likely to be biased by misclassifications of exposure to Ramadan. Under some general assumptions we can assume that the estimates were biased toward zero, and thus that the true associations were likely to have been stronger. Ramadan exposure was based on whether a period of Ramadan occurred in the 266 days before participants' births. We implicitly assumed that all Muslim women who were pregnant during Ramadan fasted, which means that we underestimated the true association with Ramadan exposure to the extent that not all pregnant Muslims fasted.

Misclassification of people who were conceived shortly after Ramadan and born prematurely could lead to further underestimation of the true association, which may predominantly affect the estimates for those who were conceived during Ramadan and for those who experienced Ramadan in

early gestation (24). If maternal fasting during Ramadan induced prematurity, part of our reported associations may be assigned to the wrong period of gestation. That is, part of the association we attributed to early exposure to Ramadan might actually be attributable to exposure during conception, and part of the association we attributed to late- and mid-gestation might actually be attributable to exposure in mid- and early gestation, respectively. If Ramadan induces prematurity and prematurity affects anthropometric measures in later life, then Ramadan-induced prematurity might be part of an explanation for our weight and BMI associations. Another limitation is that the exact birth date was unknown for 31% of the sample, and these persons were excluded. This may lead to 2 sources of bias. First, the association may differ between people who knew their birth dates and those who did not; for example, if the latter group tended to come from less educated families and effects were also stronger for such families, then associations will be underestimated and vice versa. This bias may go in both directions. Second, prenatal Ramadan exposure might affect the probability of knowing one's birth date (e.g., through effects of exposure on cognitive capacities). Consequently, people for whom the exposure had a particularly large effect may have been more likely to drop out of the sample, leading to an underestimation of the association. Finally, information on participants' own religions but not their mothers' religions was available, so we had to assume that they concurred, which may have induced minor classification error. Despite these limitations, determining prenatal exposure by using only date of birth has some advantages. It largely avoids the risk of confounding the effects of prenatal exposure to Ramadan with the effects of unmeasured characteristics of the mother (22, 24). For example, mothers who are more concerned with health may be less inclined to fast and (because of factors not related to Ramadan) may be more likely to bear healthier children. The risk of confounding prenatal exposure to Ramadan with other effects is very limited in the current approach if the assumption is met that there are no systematic differences between Muslims whose pregnancies did, versus did not, overlap with Ramadan. For example, such differences might arise when patterns of sexual intercourse are changed during Ramadan, so that parents conceiving during Ramadan have different characteristics from other parents. Previous research studying children and parents from the same wave of the Indonesian Family Life Survey that we used here demonstrated the absence of such systematic differences among parents with respect to their health, education, BMI, and other variables (24). Also, Van Ewijk (24) showed that the health of children who had been in utero during Ramadan was worse than that of their siblings. Hence, it appears that the only way in which the effects of prenatal exposure to Ramadan might be confounded with the effects of unmeasured characteristics of the mother is if mothers have better (e.g., healthier) characteristics and behaviors for some of their pregnancies than for others, and if the latter are the pregnancies that tend to overlap with a Ramadan. Therefore, the assumption seems to have been met.

Additionally, if associations between prenatal exposure to Ramadan and anthropometric measures in later life are not

caused by the observance of Ramadan itself but rather by factors coinciding with it (e.g., natural disasters, general life-style changes during public holidays), then correlations should be similar for Muslims and non-Muslims. Limitations of the analyses of non-Muslims are that non-Muslims differ from Muslims culturally and in some of their background characteristics, and that the sample size of non-Muslims in the current study was relatively low. However, the fact that we found no associations among non-Muslims between having been in utero during Ramadan and anthropometric measures in later life implies that our reported results are probably not due to coinciding influences that were also experienced by non-Muslims.

In conclusion, we found slightly reduced adult weight and height after prenatal exposure to Ramadan. Our findings may be explained by persistent stunted growth and wasting beginning in early life or by greater susceptibility to illness, leading to decreased growth and weight. Our findings have particular relevance to recommendations for pregnant Muslim women during Ramadan. As yet, there is very little research on the potential consequences of prenatal exposure to maternal fasting during Ramadan. Such studies are urgently needed to advise the large worldwide population of Muslims on potential risks of Ramadan observance during pregnancy for the later health of offspring.

ACKNOWLEDGMENTS

Author affiliations: Institute of Medical Biostatistics, Epidemiology, and Informatics, University Medical Center Mainz, Mainz, Germany (Reyn van Ewijk); Department of Economics, University of Mainz, Mainz, Germany (Reyn van Ewijk); Department of Economics, VU University Amsterdam, Amsterdam, the Netherlands (Reyn van Ewijk); Department of Obstetrics and Gynaecology, Medical Centre Alkmaar, Alkmaar, the Netherlands (Rebecca Painter); Department of Obstetrics and Gynaecology, Academic Medical Center, Amsterdam, the Netherlands (Rebecca Painter, Tessa Roseboom); and Department of Clinical Epidemiology, Biostatistics, and Bioinformatics, Academic Medical Center, Amsterdam, the Netherlands (Tessa Roseboom).

We thank Professor Maria Blettner for her helpful comments and suggestions on an earlier version of the paper.

Conflict of interest: none declared.

REFERENCES

- Harding JE. The nutritional basis of the fetal origins of adult disease. *Int J Epidemiol.* 2001;30(1):15–23.
- Koletzko B, Symonds ME, Olsen SF. Programming research: Where are we and where do we go from here? *Am J Clin Nutr.* 2011;94(6 suppl):2036S–2043S.
- Ravelli GP, Stein ZA, Susser MW. Obesity in young men after famine exposure in utero and early infancy. *N Engl J Med.* 1976;295(7):349–353.
- Ravelli ACJ, Van der Meulen JHP, Osmond C, et al. Obesity at the age of 50 y in men and women exposed to famine prenatally. *Am J Clin Nutr.* 1999;70(5):811–816.
- Stein AD, Kahn HS, Rundle A, et al. Anthropometric measures in middle age after exposure to famine during gestation: evidence from the Dutch famine. *Am J Clin Nutr.* 2007;85(3):869–876.
- Lumey LH, Stein AD, Susser E. Prenatal famine and adult health. *Annu Rev Public Health.* 2011;32:237–262.
- Chen Y, Zhou L-A. The long-term health and economic consequences of the 1959–1961 famine in China. *J Health Econ.* 2007;26(4):659–681.
- Huang C, Li Z, Wang M, et al. Early life exposure to the 1959–1961 Chinese famine has long-term health consequences. *J Nutr.* 2010;140(10):1874–1878.
- Meng X, Qian N. *The Long-Term Consequences of Famine on Survivors: Evidence From a Unique Natural Experiment Using China's Great Famine.* NBER Working Paper No. 14971. Cambridge, MA: National Bureau of Economic Research; 2009.
- Wang Y, Wang X, Kong Y, et al. The great Chinese famine leads to shorter and overweight females in Chongqing Chinese population after 50 years. *Obesity.* 2010;18(3):588–592.
- Yang Z, Zhao W, Zhang X, et al. Impact of famine during pregnancy and infancy on health in adulthood. *Obes Rev.* 2008;9(suppl 1):95S–99S.
- Ziaee V, Razaeei M, Ahmadinejad Z, et al. The changes of metabolic profile and weight during Ramadan fasting. *Singapore Med J.* 2006;47(5):409–414.
- Lamri-Senhadji MY, El Kebir B, Belleville J, et al. Assessment of dietary consumption and time-course of changes in serum lipids and lipoproteins before, during and after Ramadan in young Algerian adults. *Singapore Med J.* 2009;50(3):288–294.
- Affi ZE. Daily practices, study performance and health during the Ramadan fast. *J R Soc Health.* 1997;117(4):231–235.
- Ennigrou S, Zenaïdi M, Ben Slama F, et al. Ramadan and customs of life: investigation with 84 adult residents in the district of Tunis. *Tunis Med.* 2001;79(10):508–514.
- Sweileh N, Schnitzler A, Hunter GR, et al. Body composition and energy metabolism in resting and exercising Muslims during Ramadan fast. *J Sports Med Phys Fitness.* 1992;32(2):156–163.
- Arab M. Ketouria and serum glucose of fasting pregnant women at the end of a day in Ramadan. *Acta Med Iran.* 2004;42(3):209–212.
- Arab M, Nasrollahi S. Interrelation of Ramadan fasting and birth weight. *Med J Islam Acad Sci.* 2001;14(3):91–95.
- Joosop J, Abu J, Yu SL. A survey of fasting during pregnancy. *Singapore Med J.* 2004;45(12):583–586.
- 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(3):663–672.
- Prentice AM, Prentice A, Lamto WH, et al. Metabolic consequences of fasting during Ramadan in pregnant and lactating women. *Hum Nutr Clin Nutr.* 1983;37(4):283–294.
- Almond D, Mazumder B. Health capital and the prenatal environment: the effect of maternal fasting during pregnancy. *Am Econ J Appl Econ.* 2011;3(4):56–85.
- Alwasel SH, Abotalib Z, Aljarallah JS, et al. Changes in placental size during Ramadan. *Placenta.* 2010;31(7):607–610.
- Van Ewijk R. Long-term health effects on the next generation of Ramadan fasting during pregnancy. *J Health Econ.* 2011;30(6):1246–1260.

25. US Central Intelligence Agency. *The 2011 world factbook*. Washington, DC: Central Intelligence Agency; 2011. (<https://www.cia.gov/library/publications/the-world-factbook/geos/id.html>). (Accessed December 16, 2011).
26. Strauss J, Beegle K, Sikoki B, et al. *The Third Wave of the Indonesia Family Life Survey (IFLS3): Overview and Field Report. Working paper, WR-144/1-NIA/NICHD*. Santa Monica, CA: RAND Corporation; 2004.
27. Kieler H, Axelsson O, Nilsson S, et al. The length of human pregnancy as calculated by ultrasonographic measurement of the fetal biparietal diameter. *Ultrasound Obstet Gynecol*. 1995;6(5):353–357.
28. Wooldridge JM. *Econometric Analysis of Cross Section and Panel Data*. Cambridge, MA: MIT Press; 2002.
29. Kiziltan G, Karabudak E, Tuncay G, et al. Dietary intake and nutritional status of Turkish pregnant women during Ramadan. *Saudi Med J*. 2005;26(11):1782–1787.
30. Hermann TS, Siega-Riz AM, Hobel CJ, et al. Prolonged periods without food intake during pregnancy increase risk of elevated maternal corticotrophin-releasing hormone concentrations. *Am J Obstet Gynecol*. 2001;185(2):403–412.
31. United Nations International Children's Emergency Fund. *Tracking Progress on Child and Maternal Nutrition*. New York, NY: United Nations International Children's Emergency Fund; 2009.
32. Schmidt MK, Muslimatun S, West CE, et al. Nutritional status and linear growth of Indonesian infants in West Java are determined more by prenatal environment than by postnatal factors. *J Nutr*. 2002;132(8):2202–2207.
33. Martorell R, Khan LK, Schroeder DG. Reversibility of stunting: epidemiological findings in children from developing countries. *Eur J Clin Nutr*. 1994;48(suppl 1):45S–57S.
34. Martorell R. Results and implications of the INCAP follow-up study. *J Nutr*. 1995;125(suppl 4):1127S–1138S.