Invited Commentary: Is Prenatal Fasting During Ramadan Related to Adult Health Outcomes? A Novel and Important Question for Epidemiology

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In this issue of the Journal, Van Ewijk et al. (Am J Epidemiol. 2013;177(8):729–736) report intriguing associations between prenatal exposure to the religious month of Ramadan and body anthropometry among adult Muslims in Indonesia. They categorized prenatal exposure according to the relative timing of Ramadan and the individual’s birth date. Because the data were derived from a study of adults, they could not determine whether an individual’s mother had fasted during Ramadan or not. Therefore, they used an intention-to-treat analysis to compare the outcomes for groups categorized as unexposed with the outcomes for groups categorized as exposed during specified periods of gestation. Periconceptional exposure to Ramadan was associated with a 0.8-cm reduction in average adult height. Exposure in mid- or late gestation was associated with slightly lower adult weight. We address 5 questions raised by this study: 1) Can Ramadan fasting be considered a mild form of acute starvation?; 2) Are the findings consistent with other knowledge about prenatal nutrition and offspring outcomes?; 3) Are there other explanations for the associations that were found?; 4) Are the results internally coherent and robust enough to support the 2 main findings?; and 5) What strategies could be used to further advance this important field of research?

acute starvation; anthropometry; prenatal nutrition; Ramadan fasting

The paper by Van Ewijk et al. (1) in this issue of the Journal is an important contribution to a novel line of research on prenatal nutrition and adult health outcomes. During Ramadan, the ninth month of the Islamic lunar calendar, many Muslims follow the religious obligation to fast during the daylight hours. The ordinary (Gregorian) calendar dates of Ramadan change each year. Pregnant women can be exempted from the requirement to fast, but empirical data suggest that they usually fast along with other family members. Studies that examine whether Ramadan fasting during pregnancy influences offspring health during adulthood are directly relevant to vast numbers of Muslims across the globe. They may be relevant to non-Muslim populations, too. For example, in the United States in the 1950s and 1960s obstetricians often encouraged women to diet during pregnancy to restrict weight gain; the offspring of these women are now in midlife. Indeed, follow-up studies of adults recruited into pregnancy and birth cohorts in the United States during that time are currently investigating the influence of prenatal dietary restrictions (as well as prepregnancy obesity) on adult health (2, 3). Equally important, Ramadan studies might shed light on questions about acute prenatal nutritional deficiency and adult health outside the context of intentional daylight fasting or dietary restriction.

In an adult population whose births span many years, it is reasonable to assume that the occurrence of Ramadan while these adults were in utero was independent of decisions made by their mothers or families (i.e., exogenous). This premise for Ramadan studies was initially articulated in a paper in an economics journal (4, 5). Although the 2 authors were economists, they were well aware of prior “natural experiments” of prenatal nutrition devised by epidemiologists and had contacted one of us to discuss one such study (6). They recognized that an ordinary “natural experiment” would not suffice for studies of Ramadan because women can decide whether or not to fast during Ramadan. Because which pregnant women fasted or did not fast during the Ramadan month is generally unknown (as was the case in...
the current study), these 2 economists treated Ramadan as an exogenous variable, categorized prenatal exposure of Muslims according to the relative timing of Ramadan and the individual’s birth date, and hence used an intention-to-treat analysis similar to that of the current study (1).

Van Ewijk used a similar intention-to-treat approach in earlier work published in a health economics journal (7) and here teams up with 2 coauthors who are conducting a major ongoing epidemiologic study of adult health in cohorts exposed and unexposed in gestation to the Dutch Hunger Winter (8). Thus, this study represents a welcome step toward integration of the work being done by economists and epidemiologists. This Indonesian study included good measures of weight and height and usually self-reported birth date for a representative sample of adults drawn from a large part of the Indonesian population. Because the units sampled were households, which generally included 2 or more adults, the authors conducted within-family analyses to reduce the influence of different dietary practices across families. In accord with the basic design described above, they defined exposure for adult Muslims (the vast majority in Indonesia) according to the relative timing of Ramadan and birth date and conducted an intention-to-treat analysis. They also included a small comparison group of non-Muslim adults. The 2 main findings were 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” (1, p. 000).

We focus here on 5 questions raised by this intriguing study. First, can Ramadan fasting be considered a mild form of acute starvation? If so, Ramadan studies could offer a tractable way in which to study the relationship of acute prenatal nutritional deficiency to adult health outcomes, complementary to studies of acute famines and more generalizable to ordinary experience. We think that the current, admittedly incomplete, evidence does not favor this interpretation. Some studies of 12- to 18-hour fasting, including Ramadan fasting, have reported that metabolic changes resembling those induced by starvation occurred in pregnant but not in non-pregnant women. The term “accelerated starvation” was coined to characterize this phenomenon (9). However, the findings are not consistent across studies, and most studies were small.

Generally, the results of studies of Ramadan differ from the findings of studies of acute famine. To compare findings, we will use the results from studies of the Dutch Hunger Winter to represent famine, as they provide the best example of research on acute time-limited prenatal famine (10). Prenatal Ramadan exposure was associated with lower body mass index in this study; prenatal famine was associated with higher body mass index, mainly among women. Periconceptional exposure to Ramadan was associated in this study with smaller stature; no such evidence was observed in the famine literature. First-trimester exposure to Ramadan has been associated with lower birth weight (4); only third-trimester famine was associated with lower birth weight (11). An exception to this pattern is the association reported between early prenatal exposure to Ramadan and the increased risk of neurodisabilities (4); these latter observations are consistent with some of the Dutch Hunger Winter results (6).

Thus, at present it seems unlikely that Ramadan studies will provide answers to questions about acute prenatal nutritional deficiency outside the context of intentional daylight fasting or dietary restriction. It is even more doubtful that Ramadan studies will elucidate effects of chronic under-nutrition, although they may reveal an additional impact of Ramadan fasting within that context. Nonetheless, as noted earlier, investigations of Ramadan fasting do address questions of great importance to public health.

Second, are the findings consistent with other knowledge about prenatal nutrition, placental function, and offspring outcomes? Maternal nutrition plays an important role not only in the sustenance of pregnancy, but also in placental and fetal growth and development. Increasingly, evidence from epidemiologic studies supports the view that poor nutrition during sensitive periods of fetal growth can lead to profound and lasting changes in the growth of vital organs. This work has stimulated research on the physiological basis for a relationship between prenatal nutrition and premature onset of chronic diseases later in life (12). In animal studies, nutritional deficiencies during pregnancy have been shown to increase the risks of disease in the offspring, and in some instances, an increased risk is conferred on the next generation and possibly later generations (13, 14). Maternal undernutrition in some contexts is associated with increased risk of intrauterine growth restriction and preterm delivery, and these increased risks are at least partly mediated through the placenta. These associations among maternal (under)nutrition, role of the placenta, and aberrant fetal growth lend overall plausibility to a relationship between prenatal Ramadan fasting and offspring health during adulthood. As we discuss later, it is less clear whether the specific findings of this study are coherent with current knowledge of these relationships.

Third, are there other explanations for the associations that were found? Assuming that Ramadan per se is an exogenous variable, we think there is still some potential for bias. Thinner women tend to have smaller babies (15). It is plausible that thin women may find it easier than overweight women to fast during pregnancy (relatively lower metabolic function and lower risk of gestational diabetes among thinner women compared with heavier women), and the probability of prenatal fasting during Ramadan is likely to differ between thin and overweight women. It is also possible that Ramadan fasting may lead to behavioral changes that differ for thin and heavier women, such as in the pattern and duration of sleep or in sexual activity. These differences between thin and overweight women may vary in magnitude not only for pregnant versus nonpregnant women but also across time during pregnancy. An intention-to-treat analysis is not sufficient to rule out this kind of bias. Sensitivity analyses under various assumptions might clarify the extent to which this could (or could not) explain the main findings of the study.

Fourth, are the results internally coherent and robust enough to support the 2 main findings? One main finding was that Muslims who were conceived during Ramadan had smaller stature (as well as lower weight) than those who were unexposed to Ramadan. Notably, those exposed at any other time in gestation did not have shorter stature than

unexposed. This gestational specificity of the result lends coherence when the Muslim sample alone is considered. The results for the small non-Muslim comparison group, however, pose a dilemma. The same trend for periconceptual exposure was evident in the non-Muslim sample, though the magnitude of effect was not as large, and this result was not statistically significant. The lack of statistical significance for the trend among non-Muslims may well mean that this trend is not meaningful, but it could also be due to small sample size (the number of subjects who were conceived during Ramadan was more than 10-fold higher for Muslims (n = 1,237) than for non-Muslims (n = 110). In addition, the small size of the effect among Muslims raises some concern about the robustness of the result. The 0.8-cm reduction in adult height for those who were conceived during Ramadan months is small and therefore susceptible to the potential bias described earlier and to other bias such as measurement error (especially if measurement error differs across groups). The other main finding was that, compared with Muslims who were unexposed to Ramadan in utero, those who were exposed during mid- and late gestation had lower adult weight and similar adult height and therefore also had lower body mass index. The same trend, however, was evident for periconceptual exposure (large magnitude and statistically significant) and for early prenatal exposure (smaller magnitude and not significant). This pattern of results does not clearly support an interpretation specific to mid- and late gestation. If the result actually pertains to exposure at any time during gestation, it is rather difficult to explain in terms of reproductive biology. In this instance, however, the overall pattern of results is different for the Muslim and non-Muslim groups. In sum, we think the results are not entirely coherent, although they do provide some support for the main findings.

Notwithstanding these cautions, we believe that the new line of research represented in this study has great potential. This brings us to the final question: What strategies could be used to further advance this important field of research? We put forth 2 kinds of suggestions. One pertains to validating that Ramadan fasting has effects on offspring outcomes. Future studies could certainly improve upon the measure of exposure to Ramadan. For example, adults could be linked to birth registries that include birth dates, length of gestation, and maternal and paternal religion (in this study (1), 31% could not provide a birth date, length of gestation was unknown, and parental religion was inferred from the offspring’s religion). Prospective pregnancy cohorts that include large numbers of Muslims as well as non-Muslims followed into adulthood will be available in the near future, if not now. In these cohorts, information on maternal fasting during Ramadan would allow for a refinement of the intention-to-treat analysis by introducing approaches such as those used for instrumental variables. It could also be feasible to compare the outcomes associated with maternal and paternal exposure to Ramadan fasting in the same period. Associations specific to maternal exposure are less likely to be due to bias. This strategy has been useful in previous research on prenatal exposures, for example, in evaluating the relation of prenatal maternal smoking to offspring outcomes (16). To examine maternal versus paternal exposure to Ramadan as an exogenous variable would require sufficient numbers of offspring for whom only the mother or the father was Muslim. However, it would still be useful to examine associations for actual maternal and paternal fasting during Ramadan in these cohorts. Because not all pregnant women fast during Ramadan, and mothers and fathers may differ in religious observance if not religion per se, this is likely to be feasible. Finally, to shed more light on the coherence of the specific results of this study with other results, it would be useful to examine the associations between dietary restrictions during pregnancy and adult anthropometry in the US birth cohorts from the 1950s and 1960s mentioned earlier (3).

The other suggestion pertains to biological mechanisms. We suspect that if prenatal fasting is indeed related to the risks of chronic diseases during adulthood, the placenta plays a key role in shaping these relationships. This vital organ provides a crucial maternal-fetal interface. Therefore, in searching for mechanisms, we suggest that high priority be given to investigating the relationship of prenatal Ramadan fasting to placental development. Such studies could now go well beyond previous studies of the physiological effects of Ramadan fasting and other dietary restrictions; for example, they could include placental genes, gene expressions, and their interplay with the dietary exposure. They could also use much larger sample sizes if they are embedded within pregnancy cohorts that include substantial numbers of Muslims as well as non-Muslims.

Finally, we believe that much caution is required in the dissemination of the findings from this new line of research. This research is at an early stage, and the effect sizes in this study (1) are small. Pending further knowledge, it is, in our view, premature for public health agencies to promote changes in long established cultural practices of Ramadan fasting.


