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Short-term fetal nutritional stress and long-term health: Child height

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Abstract

Objective: This study examined the impact of in utero exposure to Ramadan, the Islamic fasting month, by trimester on height at ages 0 to 18 for a sample of children from Tehran, Iran. If exposure to Ramadan is associated with significant nutritional stress to the fetus, the fetus's adaptive responses to nutritional insufficiency could manifest as changes in height during childhood, long before any effects on aging or disease risk at older ages.

Methods: Children who were exposed and not exposed to Ramadan in utero were compared to identify any systematic difference between their parents' and households' characteristics (including height, age, education, and indicators of wealth). Also, the seasonal pattern of food consumption in Tehran was analyzed. Finally, the association of child height with prenatal exposure to Ramadan was measured, controlling for seasonality and parent and household.

Results: Ramadan associated fasting in the second trimester of gestation was associated with 0.091 age-adjusted SDs (ie, 0.60-0.67 cm) decrease in children's height at age 10 years or older. The negative association was largest in male children and was approximately 1 cm at age 12 years or older among male children.

Conclusion: Maternal Ramadan fasting in the second trimester, the critical period for long bone development, was associated with decreased height. Exposure to ritual fasting is important because approximately 75% of all Muslim children are exposed to Ramadan in utero.

1 | INTRODUCTION

A fetus may prioritize the brain to receive nutrition when facing a nutritional insufficiency (Barker, 1992; P. D. Gluckman, 2004; P. Gluckman & Hanson, 2004). The adaptive response may impact the development of other vital organs such as the heart if the nutritional insufficiency occurs during the critical windows of their development and manifest itself in higher vulnerability to heart diseases and type 2 diabetes, among others, at the middle ages or later (Barker, 1995, 1999; Barker & Osmond, 1986; Rasmussen, 2001). In addition, the critical windows of development of most vital organs closely overlap with those of the development of the long bones, which lay the foundation for future growth in height (Karimi & Basu, 2018; Khurana, 2009; Ross & Pawlina, 2011; J. M. Tanner, 1990). Accordingly, the well-established negative association of height with mortality and morbidity from different diseases may partly be attributable to the fetal nutritional environment (Barker, Osmond, & Golding, 1990; Carslake et al., 2013; Fogel, 1994; Jousilahti, Tuomilehto, Vartiainen, Eriksson, &

Puska, 2000; Waaler, 1984). Therefore, the impact of nutritional insufficiency in utero on childhood height may signal the increased risk of incidence of specific diseases later in life.

Recently published literature uses exposure to natural experiments and shows that an adverse nutrition environment during gestation is associated with a lower height. Examples of the natural experiments evaluated in the literature are cocoa price changes in Ghana, Nigerian civil war, pest attack to vineyards in France, the Dust Bowl in the United States, the Ethiopian famine, annual rainfall changes in Indonesia, and El Nino floods in Ecuador (Adhvaryu, Nyshadham, & Fenske, 2019; Akresh, Bhalotra, Leone, & Osili, 2012; Banerjee, Duflo, Postel-Vinay, & Watts, 2010; Cutler, Miller, & Norton, 2007; Dercon & Porter, 2014; Maccini & Yang, 2009; Rosales-Rueda, 2018). Only two studies have examined the impact of in utero exposure to the Islamic daytime fasting month (Ramadan), as a natural experiment, on child height. One investigation studied under 5-year-old children in 37 countries (Karimi & Basu, 2018), and another studied Indonesian adults, documenting reduced height in association with Ramadan fasting (Van Ewijk, Painter, & Roseboom, 2013). The present analysis examined the impact on height of in utero exposure to Ramadan but extends prior studies to a sample not yet studied: (a) children 5 years old and (b) Iranian children. Also, unlike prior studies assessing the impact of maternal exposure to Ramadan fasting, this study controls for both parents' height. In addition, a strength of this study is differentiating between exposure during different trimesters of pregnancy, a rare feature of early life shock analyses due to data limitations.

Even though they are exempted from Ramadan fasting, most pregnant Muslim women around the world fast during Ramadan (Almond & Mazumder, 2011; Almond, Mazumder, & van Ewijk, 2015; Oosterbeek & van der Klaauw, 2013; Ziaee et al., 2010). While actual fasting is believed to be the main mechanism of the potential effect of Ramadan on a fetus, other mechanisms likely play a role as well. For example, it may disrupt routine nutritional intake during pregnancy because restaurants are usually closed during the daytime in Ramadan, as are workplace food courts and cafes in Muslim countries. In addition, pregnant women usually avoid eating in the presence of fasting members of the household out of respect or postpone eating warm meals until fasting members of the household eat at sunrise or sunset. Food preparation for fasting members of the household, especially the predawn meal (*sahari*, *sahri*, or *sahur*), can disrupt sleeping patterns during pregnancy and potentially affect fetal health.

2 | MATERIALS AND METHODS

2.1 | Data collection

Data were collected in October 2011 using an Urban Health Equity and Assessment Response Tool (Urban HEART) from Tehran, Iran. The survey was designed by the World Health Organization, WHO, Center for Health Development and conducted by the Municipality of Tehran. The purpose of the survey was to assess the city's residents' physical, mental, social, and environmental health and their health habits, diet, access to health care services, and overall quality of life. Data were collected using a stratified multistage cluster probability sampling method, including representative samples of households from all 22 districts of the city. 33 915 households, including 118 464 individuals, were surveyed. The survey data included individual-level socioeconomic status indicators, date of birth (DOB), and height in cm. The DOB of 22 350 individuals was not reported, and they were excluded resulting in 96 114 individuals remaining.

Children (0-18 years) were identified, allowing control for parental height (ie, the hereditary component) (Silventoinen et al., 2003). Also, children's birth dates are consistent compared to adults for whom there are inconsistencies in recording birth dates. Misrecoreded DOBs were prevalent in Iran before the early 1990s for two reasons. First, for a disproportionally large number of those born before the late 1970s (16% to 22% in different years), the reported birth month is the first Persian month, *Farvardin*, spanning from March 21 to April 20, probably related to out-of-hospital births. After the 1970s, the proportion of births during *Farvardin* becomes less than 10%. Second, a disproportionally large number of those born from the mid-1960s to the early 1990s (14% to 22% in different years) were reported to have been born in the sixth Persian month, *Shahrivar* (August 23 to September 22), which is related the month prior to the start of school. Primary schools enroll children who are at least 7 years old by the 31st of *Shahrivar*. Children born in the next month or later must start the school next year, and parents of children born in the second half of a year are incentivized to claim that the children's birth took place in the first half of the year. Until the country's national registration office required a hospital birth certificate in the late 1980s and started to enforce the requirement in the early 1990s strictly, the distribution of recorded births across months was skewed. Consequently, 1993 is the last year in which birthdates are clustered in *Shahrivar*. To minimize errors in birth month, children born before the seventh Persian month of 1993 were excluded, resulting in 22 122 children for inclusion (Figure 1).

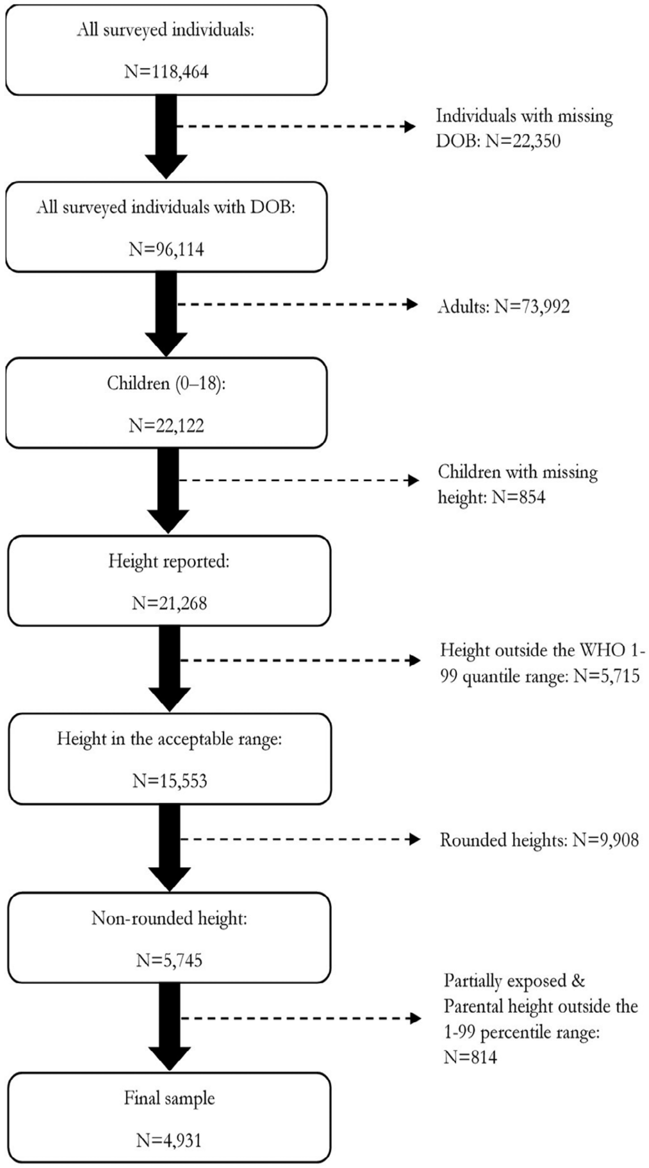

FIGURE 1 Data refinement procedure

Among 22 122 children, height was not reported for 854, reducing to the sample to 21 268 children with DOB and height information. According to the survey's questionnaire, child height is based on either direct measurement by interviewers or interviewees' accounts. Measured heights were used in the present analysis. This resulted in 73% of 21 268 children being excluded in analyses to focus on the most reliable reported heights. First, children whose height was an outlier were excluded from analyses using acceptable height ranges (1st and 99th percentiles) based on sex- and age-specific percentile data, excluding 5715 children. Of the remaining 15 553 children, 9808 were excluded because their height was rounded to the nearest 5 or 10 cm. Therefore, the initial analytical sample included 5745 children (Figure 1). Height measurement error could not be estimated because there were no replicate measures. This sample size was further reduced to 4931 because of missing values in parental height and to exclude children who were partially exposed to Ramadan (see Section 2.2).

Elimination of nearly three quarters (73%) of children potentially introduces possible sample selection bias. Based on household characteristics, the sub-sample analyzed was not statistically significantly different from the total sample (Table A1). In addition, height reporting accuracy was not correlated with household wealth indicators (ie, homeownership and home size, and city district of residence (Table A1 and Figure A1), and seemed random with respect to characteristics analyzed.

The Statistical Center of Iran's annual Household Expenditure and Income Surveys (HEIS) were used to extract the trends in Tehrani households' food consumption from 1992 to 2011. HEIS are cross-sectional surveys in which household expenditures on about 1100 items are reported. The items are categorized based on the United Nations' Classification of Individual Consumption by Purpose (COICOP). Among them, about 240 are related to food consumption. Since the HEIS started to report households' city of residence from 1998, HEIS data from 1998 to 2011 (14 years) were selected. During the period, 17 758 Tehrani households were surveyed (Table A3). Based on the HEIS, total expenditures on foods were calculated. Then, total food expenditures were adjusted for inflation using the Central Bank of Iran's consumer price index, CPI (with the base year of 2011). Next, sampling weights were applied, and average food expenditures were calculated by survey season. Calculated average expenditures were transformed from Rial (the formal unit of currency) to 1000 Iranian tomans (TIT), which is commonly used by and easily understood among Iranians. Units in TIT are easily comparable with the US dollar: in 2011, 1 TIT was equivalent to 1.2 USD. Lastly, average expenditures using 2-year moving averages were calculated for smoothing, as the number of households per season was small, especially in 2009.

2.2 | Measuring prenatal exposure to Ramadan

Gestation during Ramadan was estimated by counting backward from the child's exact DOB. A normal gestation period of 270 days (38 weeks) was assumed for all children. If the estimated gestation coincided with Ramadan, then days of overlap were calculated. Next, the hours of exposure to Ramadan (equal to daylight hours) during each day of gestation overlap with fasting were calculated. Total daylight hours during exposure to Ramadan fasting provide an estimate of exposure of the fetus to fasting because Ramadan, a month on the Arabic lunar calendar, varies based on the solar calendars, including the Persian calendar. Ramadan starts approximately 11 days earlier each year. Hence, daylight hours during Ramadan can vary substantially in Tehran, which is located at a relatively high northern latitude of 35.69°N, with variation in daylight hours between 9.7 and 14.6 hours in a year. Also, since fetal growth varies in rate during different trimesters of gestation (Little, 2009; J. M. Tanner, 1990), gestation was broken down into three trimesters, then total hourly exposure for each trimester was calculated.

Three groups of children were defined: those whose presumed 38-week gestation (a) included a full 30-day Ramadan (b) partially coincided with Ramadan during the birth or conception month, and (c) did not coincide with Ramadan. According to a World Health Organization research, in 2010, approximately 12.9% of pregnancies in Iran lasted 37 weeks or less (WHO, 2016). Assuming the same rate of premature birth applies to this study's analysis sample, whether or not a child was exposed to Ramadan was misassigned by at least 1 week for an estimated 12.9% of children. To account for a potential misassignment of exposure to Ramadan, children whose presumed 38-week gestation age coincided with Ramadan during the estimated conception month were excluded from the analysis sample because part of them might not have been ever exposed to Ramadan due to preterm birth. For a sharper comparison between the exposed and non-exposed, those who were partially exposed to Ramadan during their birth month were also excluded. These final exclusion criteria plus accounting for extreme abnormality in parental heights (ie, heights falling outside the WHO first-99th percentile range) reduced the analytical sample size to 4931 children (Figure 1). However, children whose parental heights were rounded to the nearest 5 cm were not excluded to preserve sample size.

2.3 | Identification assumptions

Variation in the timing of exposure to Ramadan fasting during trimesters of gestation was used to measure the association of nutritional stress in utero and children's height. Observance of Ramadan is endogenous, and the coincidence of pregnancy with Ramadan may be considered exogenous. Hence, exposure to Ramadan provides an opportunity to approximate an association similar to an "intent to treatment" trial.

Identification of the association also relies on the assumption that an overlap of pregnancy with Ramadan fasting does not change gestation length. Available data do not provide information on date of conception or date of the last menstrual period, obviating an estimation of pregnancy lengths. Nonetheless, evidence from other studies shows that Ramadan-induced nutritional stress does not affect gestation length (Almond & Mazumder, 2011; Karimi, 2017).

2.4 | Statistical model

The linear association of prenatal exposure to Ramadan fasting and height-for-age z-score was analyzed using the following statistical model of:

$$\begin{aligned} HAZ_i = {} & \alpha + \theta_1 Exposure_{i,trimester1} + \theta_2 Exposure_{i,trimester2} \\ & + \theta_3 Exposure_{i,trimester3} + \beta_1 BirthYear_i \\ & + \beta_2 BirthMonth_i + \varphi AgeDays_i + \sigma Sex_i \\ & + \varphi_1 MotherAge_i + \varphi_2 FatherAge_i + \eta_1 MotherHeight_i \\ & + \eta_2 FatherHeight_i + \epsilon_1 MotherEducation_i \\ & + \epsilon_2 FatherEducation_i + \rho_1 HomeOwn_i \\ & + \rho_2 HomeArea_i + \delta CityDistrict_i + \varepsilon_i \end{aligned}$$

where i indicates a child. HAZ is the child's height-for-age z-score. $Exposure_{trimester_j}$ is total hours of exposure to Ramadan during trimester j (j=1, 2, 3) of gestation, and ranges from 0 to 406 hours. *BirthYear* and *BirthMonth* are the child's birth year (1993-2011) and birth month (1-12). *AgeDays* is the child's age in days, calculated from the child's DOB and interview date. *Sex* indicates the child's sex. Parental age, *MotherAge* and *FatherAge*, were measured in years. Parental heights, *MotherHeight* and *FatherHeight*, were measured in centimeters. Parental education, *MotherEducation* and*FatherEducation*, were categorized in five groups: illiterate, some primary school, some secondary school, some high school, and some college. Homeownership status, *HomeOwn*, is either owned or rented. *HomeArea* is square meters (m^2) of household residence. *CityDistrict* (range: 1 to 22) indicates city district of residence location.

Height is sex- and age-dependent, but sample size concerns did not allow for conducting age-specific analyses for each sex. Hence, the height was adjusted. An appropriate transformation is the computation of sex- and age-specific height z-scores (HAZ) using age- and sex-specific means and SDs from WHO (month). Transformation of all heights to sex-age-specific z-scores (SDs from the median) allows pooling children data regardless of sex and age.

Year of birth controls for year-specific effects, as the country has experienced a secular trend of increasing adult height in the past four decades (Bentham & Ezzati, 2016). Controlling for the effect of seasonality is especially important because Ramadan occurs 11 days earlier each year. Hence, birth month is added to granularly control for seasonal effects on child height (Costa, Helmchen, & Wilson, 2007; Weber, Prossinger, & Seidler, 1998). Year and month of birth were analyzed separately. Children in this study were exposed to 19 Ramadan fasting cycles occurring from July 31 to March 24, a period that includes most of the summer, the entire autumn and winter, and a few days of spring.

Parental height controls for the contribution of genetics. Parental education, especially mother's education, controls for behavior during pregnancy (Behrman & Deolalikar, 1988; Thomas, Strauss, & Henriques, 1991). Homeownership, home area in meters^2, and the city district account for the well-documented relationship between height and household wealth (Case & Paxson, 2008; Mankiw & Weinzierl, 2010).

The linear regression method, which minimizes the sum of squared errors (the differences between the observed and predicted *HAZ*), used to estimate the model. The association of hours of exposure with Ramadan during trimesters of gestation (θs) were estimated in a stepwise fashion: birth year, birth month, age in days, sex, parental height, age, and education, city district, and residence information (ownership and area) were added gradually to the statistical model. In all estimations, SEs were clustered at the city district level. Statistical significance levels changed only slightly if different clustering variables were used (eg, birth year, birth month, year-specific birth month, sex). The statistical package used for analyses was STATA 15.0 (STATA, Inc, College Station, Texas).

3 | RESULTS

3.1 | Testing if exposure to Ramadan is endogenous

Descriptive statistics of children in the study, stratified by the status of exposure to Ramadan, did not indicate selection into or out of Ramadan (Table 1). In addition, examining whether exposure to Ramadan during any given trimester associated with specific parental/household characteristics (controlling for other characteristics) did not indicate a systematic selection of pregnancy into or out of Ramadan (Table A2). Exposure to Ramadan during different trimesters of gestation was not correlated with parental or household characteristics, with exceptions of (1) maternal education and (2) homeownership status. Mothers who had a college degree compared with those who had no education, the likelihood of exposure during the first trimester increased, but that during the second trimester decreased. Hence, education was not a source of systematic selection bias. Homeownership decreased the likelihood of the first trimester of pregnancy overlap with Ramadan (by about 3.7 percentage points). Other indicators of household wealth were not

TABLE 1 Descriptive statistics of characteristics of children by the status of exposure to Ramadan during gestation

	No exposure	Full exposure
N	1554	3377
Hours of exposure to Ramadan		
Average	0	328
SD	0	29
Median	0	324
Height-for-age *z*-score		
Average	−0.017	−0.002
SD	1.114	1.080
Median	0.006	−0.019
Father's age (year)		
Average	44	44
SD	9	9
Median	43	43
Mother's age (year)		
Average	38	38
SD	8	8
Median	38	38
Father's education		
% Illiterate	3.4	3.6
% Some primary or secondary	23.6	23.7
% Some high school	47.7	46.8
% Some college	25.4	25.9
Mother's education		
% Illiterate	3.9	4.2
% Some primary or secondary	20.3	21.2
% Some high school	55.2	53.5
% Some college	20.7	21.0
% Owns the place of residence	58.9	57.7
Area of place of residence (m^2)		
Average	93	92
SD	70	68
Median	80	76
City district		
% in high income district	17.4	18.7
% in middle income district	46.0	45.8
% in low income district	26.8	25.6

Source: Tehran Urban HEART 2011, Municipality of Tehran.

correlated with exposure to Ramadan. If observable indices of wealth do not capture all the variation in wealth, then any adverse effect of prenatal exposure to Ramadan on height may be partly overestimated, because children of wealthier parents tend to be taller.

No systematic selection in or out of participation in Ramadan fasting was found in other Ramadan studies, which examined other outcomes, as well (Almond & Mazumder, 2011; Greve, Schultz-nielsen, & Tekin, 2015; Karimi & Basu, 2018; Majid, 2015).

3.2 | Assessing the seasonal pattern of food consumption in Tehran

A seasonal pattern in Tehrani's food consumption was evident from 1999 until 2005: food expenditures in autumn and winter were typically greater than in the spring or summer (Figure 2). Also, the difference in food expenditures in the first and second half of the year was statistically significant. In contrast, from 2006 onward, seasonal variation in Tehrani households' food expenditures was not substantial. The overall trends in food expenditures from 2005 to 2009 followed the trends in household income (Figure A2). Specifically, household income decreased by about 20% from late 2007 to late 2009, then started a gradual increase towards its previous level until early 2012. The trend in household income, in turn, was associated with the country's general economic trend, measured by the gross domestic product (Figure A3).

The statistical model, which included birth year and month as covariate regressors, accounts for the observed seasonal variation in food consumption. Season-specific predicted and actual food expenditures for Tehrani households were graphed, showing the effect of birth month and year, and the predicted trends followed the observed data (Figure 3). Other factors, including Ramadan, are responsible for observed unexplained variation by year and season in food consumption. This variation was used to isolate the effect of Ramadan, after controlling for an array of individual- and household-level covariate factors.

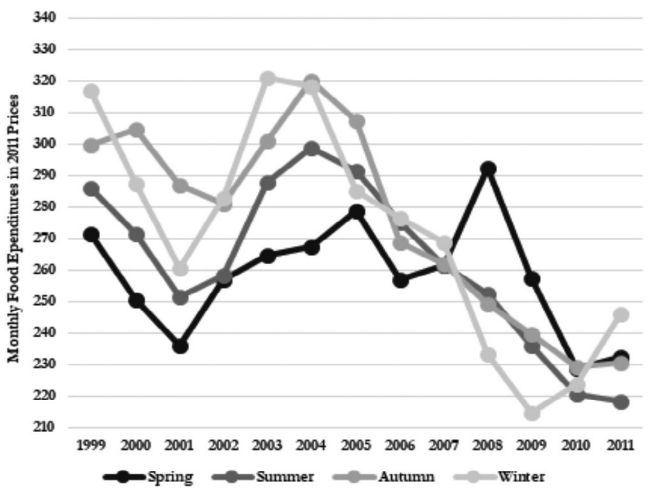

FIGURE 2 Tehrani household's total monthly food expenditures (two-year moving averages) in 2011 prices by season of interview, values in 1000 Iranian toman (TIT)—about 1.2 USD in 2011. *Note*: Authors' calculations. *Source*: Iran's Household Expenditure and Income Survey (HEIS), 1998 to 2011

3.3 | Main results

The stepwise estimation method identified the most influential background factors. The estimated θs, were multiplied by 11.4 hours × 30 days to obtain an estimate of the effect of a full exposure to Ramadan (Table 2). 11.4 is the average hours per day of daylight in a typical Ramadan fasting day for exposed children in the sample. Typically, Ramadan has 30 days, and it rarely has 29 days.

With no control variables included, none of the regression estimates of the associations of *HAZ* and the measures of exposure to Ramadan were statistically significant. As covariates were added to control for potential confounders in the base-line regression, birth month emerged as the most influential covariate, highlighting the importance of controlling for seasonality in the Ramadan context (Table 2, column 3). After controlling for birth year and month, the inclusion of other covariates did not substantially change the results (Table 2, columns 4-10). This indicates that exposure to Ramadan may not be significantly linearly confounded by parental and household characteristics.

Another key takeaway message in the regressions is that exposure to Ramadan during the second trimester of gestation was statistically significantly associated with lower *HAZ* (Table 2). Expectedly, the second trimester of gestation has the greatest overlap with the critical windows of development of the long bones. In the fully controlled model (Table 2, column 10), exposure to Ramadan 29 to 30 days during the second trimester was associated with an average 0.091 SDs decrease in height. Stratifying regression estimates by sex showed that male children were more affected than females. Exposure to Ramadan 29 to 30 days during the second trimester was associated with an average decrease in male child height of 0.135 SDs (Table 3, column 9).

Estimated association *z*-scores (*HAZ*) were converted to centimeters, using the sex- and age-specific SDs of height in the WHO reference population. In Figure 4, the estimated association of decreased height with Ramadan fasting from the fully controlled regressions (column

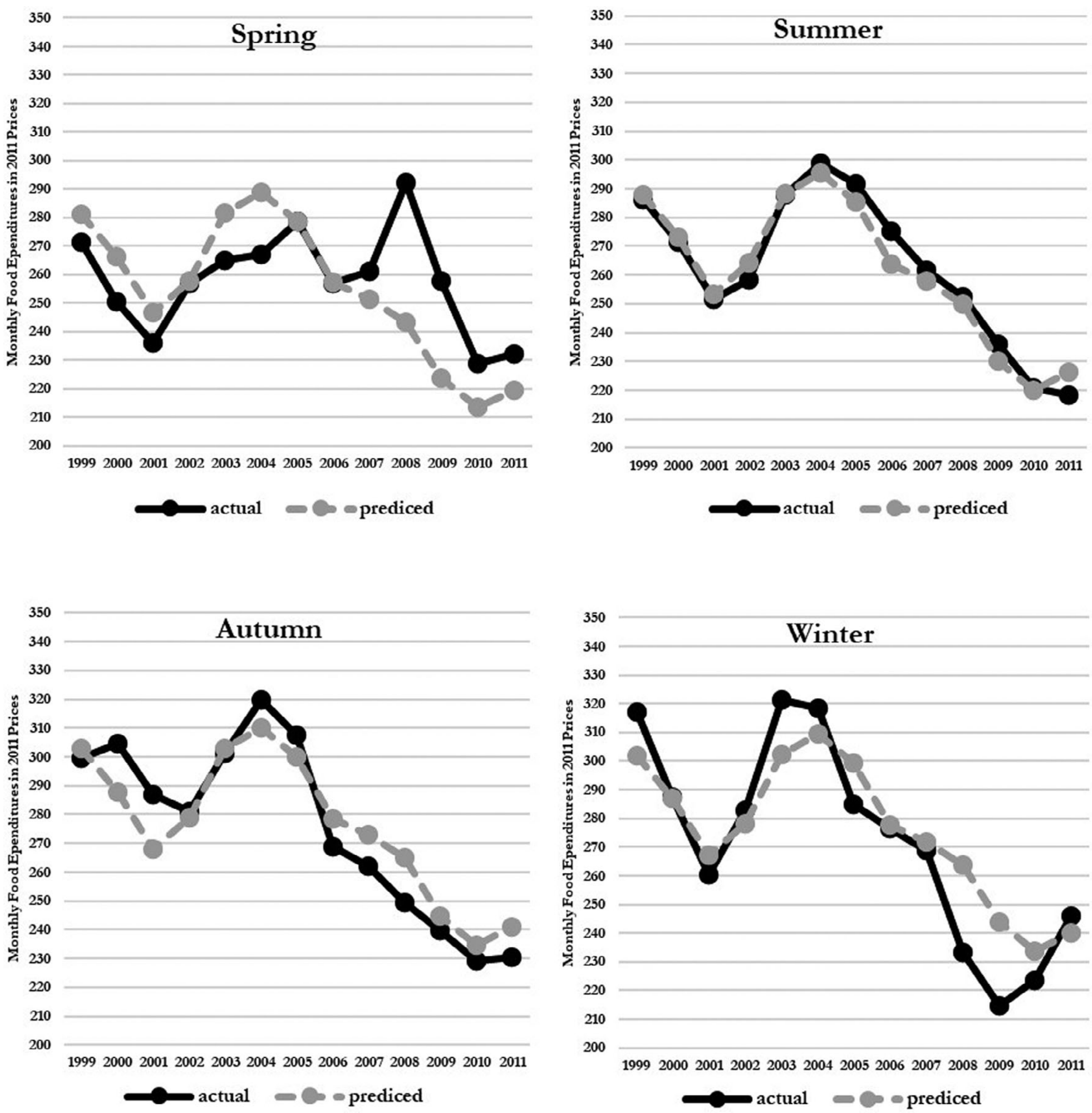

FIGURE 3 Actual vs Predicted: Tehrani household's total monthly food expenditures (two-year moving averages) in 2011 prices by season of interview, values in 1000 Iranian toman (TIT)—about 1.2 USD in 2011. *Notes*: Predicted values are those of a linear regression of food expenditures on survey year and season. *Source*: Iran's Household Expenditure and Income Survey (HEIS), 1998 to 2011

10 in Table 2, columns 9 and 18 in Table 3) were used. Overall and the sex- and age-specific associations of height (cm) with exposure to Ramadan fasting during the second trimester was statistically significant.

A distinct pattern of association of height with second-trimester exposure to Ramadan was found. The overall (combined sexes) magnitude of reduction in height was small at younger ages when the height is shorter and variation in height is also small. As age increases, the dispersion of height is greater at older ages and plateaued at approximately 15 years. Therefore, the estimated overall mean reduction of 0.091 *z*-scores (column 10 in Table 2) translates to 0.20 to 0.67 cm, depending on age.

The same pattern was observed for male and female children, although the point estimates were statistically insignificant for females. In summary, the negative associations for under 1-year-old male and female child height were 0.29 cm and 0.13 cm, respectively. The associations, however, increased to about 1.05 cm and 0.40 cm at age 15 years among male and female children, respectively.

4 | DISCUSSION

This analysis showed the importance of accounting for seasonality (Table 2, column 3) and investigated

TABLE 2 The effect of a full 30-day exposure to Ramadan on height-for-age *z*-score, both sexes

Variable	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
N	5745	5745	5745	5745	5745	4947	4947	4941	4938	4931
Hours of exposure	−0.004	−0.009	0.013	0.013	0.014	0.004	0.008	0.015	0.015	0.017
in trimester 1	(−0.086, 0.078)	(−0.089, 0.071)	(−0.075, 0.101)	(−0.075, 0.101)	(−0.074, 0.102)	(−0.080, 0.108)	(−0.086, 0.102)	(−0.079, 0.109)	(−0.079, 0.109)	(−0.077, 0.111)
Hours of exposure	−0.058	−0.061	−0.087*	−0.087*	−0.087*	−0.088*	−0.087*	−0.091*	−0.092*	−0.091*
in trimester 2	(−0.138, 0.022)	(−0.141, 0.019)	(−0.179, 0.005)	(−0.179, 0.005)	(−0.179, 0.005)	(−0.186, 0.010)	(−0.185, 0.011)	(−0.189, 0.007)	(−0.190, 0.006)	(−0.189, 0.007)
Hours of exposure	−0.031	−0.042	−0.001	−0.001	−0.004	−0.025	−0.027	−0.022	−0.020	−0.022
in trimester 3	(−0.113, 0.051)	(−0.122, 0.038)	(−0.089, 0.087)	(−0.089, 0.087)	(−0.092, 0.084)	(−0.119, 0.069)	(−0.121, 0.067)	(−0.116, 0.072)	(−0.114, 0.074)	(−0.116, 0.072)
Controls										
Birth year		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Birth month			Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Age in days				Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sex					Yes	Yes	Yes	Yes	Yes	Yes
Parental height						Yes	Yes	Yes	Yes	Yes
Parental age							Yes	Yes	Yes	Yes
Parental education								Yes	Yes	Yes
City district									Yes	Yes
Home (ownership and area)										Yes

Note: Each set of the associations under columns (1) to (10) in a column was calculated using the result of estimating a regression in which the left-hand-side variable is height-for-age *z*-score and the right-hand-side variables are total hours of exposure to Ramadan during trimesters of gestation and control variables, listed in the bottom part of the table. The control variables were gradually added. Then, the estimated coefficients of the exposure measures, representing the effect on the height-for-age z-score of an hour of exposure were multiplied by 342 (=11.4 × 30, 11.4 is the average daylight hours in a Ramadan day for an exposed individual in the sample). SEs were clustered at the city district level. Numbers in parentheses represent 95% confidence intervals.
Source: (*Data*) Tehran Urban HEART 2011, Municipality of Tehran.
*Indicate the statistical significance level at the 1%.

the seasonal variation in food consumption in Tehran. The seasonal patterns were not unique to Tehran, as similar seasonal patterns were documented in the country's urban areas, including 200 962 households (Table A4 and Figure A4). The seasonal patterns were accounted for in the statistical analysis. The analyses also controlled for the cohort effect with the year of birth. The age effect was controlled in two ways. First, children's age in days was included among the covariates. Secondly, the measured effects are valid regardless of age because height-for-age *Z*-score was used as the dependent variable. The effect (in centimeters) was more pronounced in older children because of greater variation in older children's height, and a possible cumulative effect. Similarly, a rare study that used a randomized control trial (RCT) to assess the effect of nutrition during pregnancy on children's height found that the height difference of children whose mothers received nutritional supplementation during pregnancy and children of those who did not was statistically insignificant by age 2. However, the difference became larger and statistically significant as children grew older (Kusin, Renqvist, Kardjati, & Houtkooper, 1992), suggesting a cumulative effect.

The effect sizes measured in this study are probably smaller than the actual impact of fasting during pregnancy because it is very unlikely that all Tehrani pregnant women in the analysis sample fasted. One study, performed in a hospital in Tehran in 2004 (N = 189), showed 35% of women never fasted during Ramadan, and 14% fasted for less than 10 days (Ziaee et al., 2010).

TABLE 3 The effect of a full 30-day exposure to Ramadan on height-for-age z-score, sex-specific results

Males	**(1)**	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**	**(9)**
N	2794	2794	2794	2794	2391	2391	2388	2387	2384
Hours of exposure	0.049	0.072	0.086	0.086	0.077	0.074	0.082	0.084	0.092
in trimester 1	(−0.071, 0.169)	(−0.046, 0.190)	(−0.043, 0.215)	(−0.043, 0.215)	(−0.060, 0.214)	(−0.063, 0.211)	(−0.055, 0.219)	(−0.053, 0.221)	(−0.045, 0.229)
Hours of exposure	−0.076	−0.077	−0.087	−0.087	−0.096	−0.104	−0.121	−0.139*	−0.135*
in trimester 2	(−0.194, 0.042)	(−0.195, 0.041)	(−0.220, 0.046)	(−0.220, 0.046)	(−0.241, 0.049)	(−0.249, 0.041)	(−0.266, 0.024)	(−0.284, 0.006)	(−0.280, 0.010)
Hours of exposure	−0.001	0.043	0.033	0.033	0.011	0.002	−0.006	−0.003	−0.002
in trimester 3	(−0.124, 0.122)	(−0.079, 0.165)	(−0.098, 0.164)	(−0.098, 0.164)	(−0.130, 0.152)	(−0.139, 0.143)	(−0.147, 0.135)	(−0.144, 0.138)	(−0.143, 0.139)
Females	**(10)**	**(11)**	**(12)**	**(13)**	**(14)**	**(15)**	**(16)**	**(17)**	**(18)**
N	2951	2951	2951	2951	2556	2556	2553	2551	2547
Hours of exposure	−0.056	−0.061	−0.064	−0.064	−0.074	−0.060	−0.056	−0.058	−0.059
in trimester 1	(−0.168, 0.056)	(−0.173, 0.051)	(−0.186, 0.058)	(−0.186, 0.058)	(−0.203, 0.055)	(−0.189, 0.069)	(−0.185, 0.073)	(−0.187, 0.071)	(−0.188, 0.070)
Hours of exposure	−0.040	−0.047	−0.089	−0.089	−0.083	−0.073	−0.066	−0.059	−0.058
in trimester 2	(−0.150, 0.070)	(−0.157, 0.063)	(−0.214, 0.036)	(−0.214, 0.036)	(−0.216, 0.050)	(−0.204, 0.058)	(−0.197, 0.065)	(−0.192, 0.074)	(−0.191, 0.075)
Hours of exposure	−0.064	−0.014	−0.045	−0.044	−0.062	−0.057	−0.051	−0.056	−0.058
in trimester 3	(−0.174, 0.046)	(−0.122, 0.094)	(−0.165, 0.075)	(−0.164, 0.076)	(−0.189, 0.065)	(−0.182, 0.068)	(−0.176, 0.074)	(−0.183, 0.071)	(−0.185, 0.069)
Controls									
Birth year		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Birth month			Yes	Yes	Yes	Yes	Yes	Yes	Yes
Age in days				Yes	Yes	Yes	Yes	Yes	Yes
Parental height					Yes	Yes	Yes	Yes	Yes
Parental age						Yes	Yes	Yes	Yes
Parental education							Yes	Yes	Yes
City district								Yes	Yes
Home (ownership and area)									Yes

Note: Each set of the associations under columns (1) to (18) was calculated using the result of estimating a regression in which the left-hand-side variable is height-for-age z-score and the right-hand-side variables are total hours of exposure to Ramadan during trimesters of gestation and control variables, listed in the bottom part of the table. The control variables were gradually added. Then, the estimated coefficients of the exposure measures, representing the effect on the height-for-age z-score of an hour of exposure, were multiplied by 342 (=11.4 × 30, 11.4 is the average daylight hours in a Ramadan day for an exposed individual in the sample). SEs were clustered at the city district level. Numbers in parentheses represent 95% confidence intervals.
Source: (*Data*) Tehran Urban HEART 2011, Municipality of Tehran.
*Indicate the statistical significance level at the 1%.

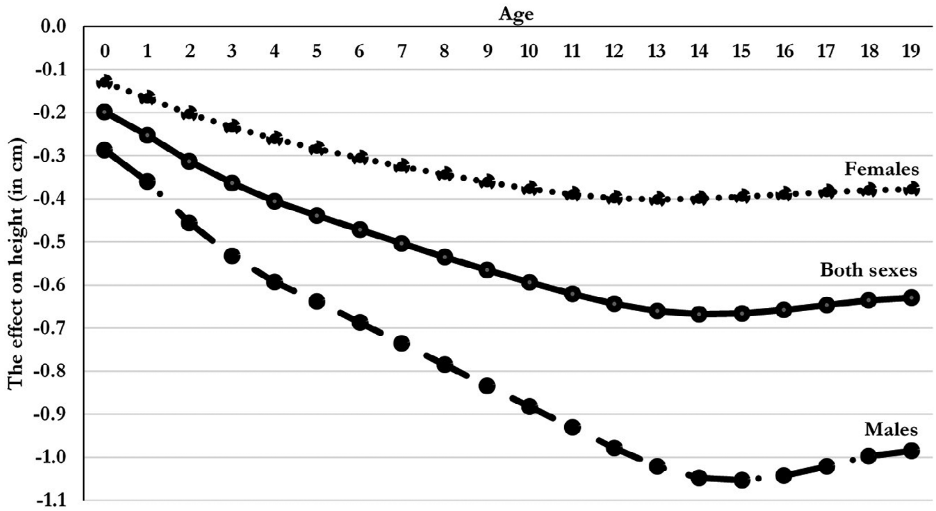

FIGURE 4 The effect of a full 30-day exposure to Ramadan during the second trimester of gestation on height in centimeters. *Note*: The figure presents sex- and age-specific effects on the height of full-30 day exposure to Ramadan during the second trimester of gestation. To find each point on this figure, the corresponding coefficient in Table (3) or (4), that is, the effect on *z*-score, is multiplied by the WHO reference population SD of height that corresponds to the age and sex. *Source*: (*Data*) Tehran Urban HEART 2011, Municipality of Tehran

The mean for number fasting days was 13 days. Therefore, the actual impact on the child height of full-time fasting may be 2-fold higher than that measured in the present study. Also, no significant difference was found between the proportion who had a history of abortion in the non-fasting and fasting mothers (Ziaee et al., 2010).

The estimated associations persisted after adjustment for numerous covariates. Alternative measures of exposure (ie, days of exposure and simple 0/1 indicators of exposure) resulted in similar point estimates. Adding partially exposed individuals to the analytical sample only slightly changed the point estimates. Moreover, the inclusion of other measures of household wealth (eg, number of rooms in the household dwelling, ownership of a car, and access to the internet) did not change the results. Finally, second-order moving average analyses of seasonality did not substantially affect the results.

The association of Ramadan fasting and reduced child height in this study is consistent with previously published findings, and the estimated effect size is comparable to that previously estimated by Karimi and Basu (2018). These prior studies reported that full exposure to Ramadan during the second trimester of gestation is associated with a mean 0.5 cm decrease in height among 4-year-old Muslim male children. The estimate in the present study for the same effect for the 4-year-old male children was 0.6 cm. The prior study of Ramadan and height, however, found that exposure to Ramadan during the month of conception (not the second trimester) was associated with decreased height in adulthood (Van Ewijk et al., 2013), with an estimated effect size of 0.8 cm.

This study's findings are in the range of the findings of studies that examined mild nutritional shocks. eg, the effect of a 40% income decrease caused by an insect (Phylloxera) attack on French vineyards on heights of 20-year-old males born during the period was estimated 0.2 cm (Banerjee et al., 2010). As another example, a 20% rainfall increase in rural Indonesia in the birth year was associated with an estimated 0.6 cm increase in height among 26- to 47-year-old women, but there was little indication that the adult male height was affected by birth year rainfall (Maccini & Yang, 2009). However, the effect size measured in this study is smaller than that associated with prenatal exposure to moderate or intense nutritional shocks such as famines and severe floods. For example, the effect size of the Dutch Famine on adult men and women's height was 3.2 cm and 4.5 cm, respectively (Portrait, van Wingerden, & Deeg, 2017). A study of Chinese born during the 1959 to 1961 famines reported an effect size of 1.3 cm to 1.7 cm among 32-year-old women who were exposed to the famine in their birth year (Huang, Li, Wang, & Martorell, 2010). Also, Ecuadorian male and female children (pooled) from poor families that were exposed to the 1997 to 1998 year-long El Niño floods in utero were approximately 3.5 cm shorter in stature by 5 years later (Rosales-Rueda, 2018) (Figure 5).

A smaller association, not statistically significant, between prenatal exposure to Ramadan and female child height is consistent with analyses of the effect of Ramadan fasting on height in girls (Karimi & Basu, 2018). The finding that males were more affected by Ramadan fasting during the second trimester is generally consistent with

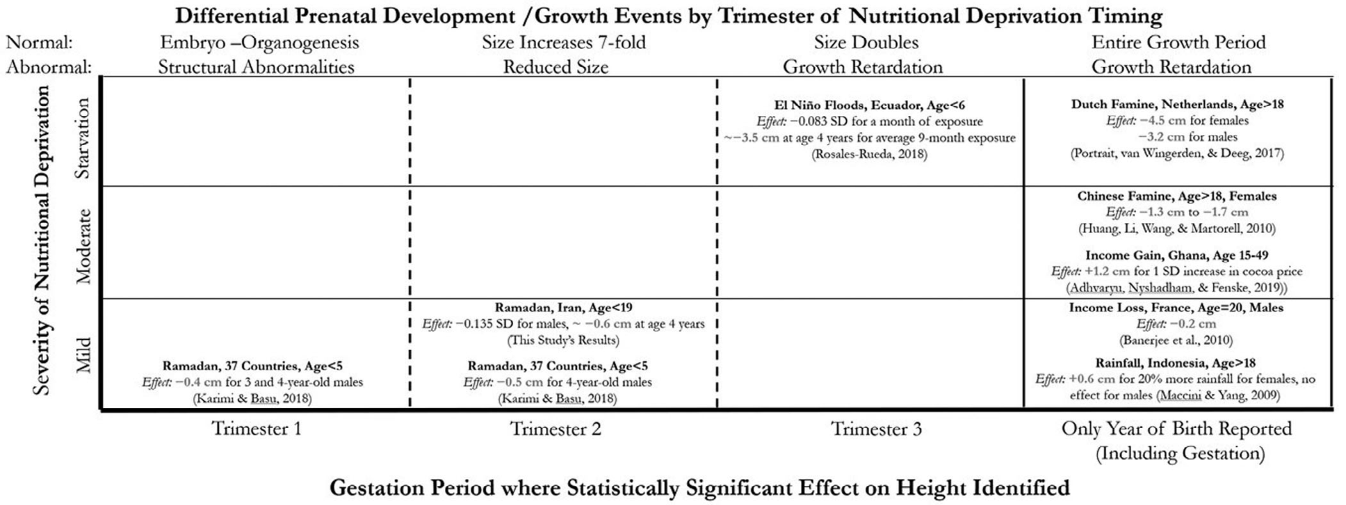

FIGURE 5 The severity of nutritional deprivation shock and exposure period in pregnancy. *Note*: Congenital anomalies could be included here, but the cited studies did not report birth defects

analyses of child growth that found males are more vulnerable than females to the effect of prenatal and postnatal nutritional and non-nutritional stresses (Almond & Mazumder, 2011; Fukuda, Fukuda, Shimizu, & Møller, 1998; Hansen, Moller, & Olsen, 1999; Lyster, 1974; Zorn, Sucur, Stare, & Meden-Vrtovec, 2002). The association of reduced height among girls is not statistically significant (Table 3, columns 10-18) are also consistent with previously published research that found females exhibit smaller effects of environmental changes, whether the effects are positive or negative (Stinson, 1985). It is also possible that the size of the sex-specific samples was not large enough to have statistical power for the identification of small-size effects, perhaps confounded by measurement error. A differential response, such as minor deceleration, among females and better recovery through catchup growth may explain gender differences in response to nutritional deprivation.

The statistically significant association between decreased child height and exposure to Ramadan fasting during the second trimester of gestation is consistent with the timing of critical window of development for the long bones (Ross & Pawlina, 2011; J. M. Tanner, 1990). Nonetheless, identifying an association in the second trimester is interesting because it is an example wherein human plasticity is not detected. Plasticity in human growth is "…the potential for growth [that] is inherited but remains latent under less favorable circumstances" and "…it may be possible to increase or retard growth of the human body by modification of the environment" (Kaplan, 1954). Human plasticity includes catchup growth that occurs when environmental circumstances (health, nutritional) improve following deprivation (Prader, Tanner, & von Harnack, 1963). Catchup growth is limited or prevented with prenatal exposure to teratogens, feto-toxic substances, and malnutrition (micronutrient, protein-calorie, or calorie deficient). Prenatal environmental insults can permanently alter the genetic program for prenatal growth and development (Holmes, 1992).

The persistence of the negative association of child height with exposure to Ramadan in the second trimester is a case in which limits of human growth plasticity are reached, and catchup growth did not overcome the deficit related to Ramadan fasting by pregnant women. Nutritional deprivation during the second trimester was associated with growth deficits that were not reversed prenatally after fasting ended, or postnatally, which implies a fetal imprinting effect (Lambertini, 2014). Findings in the present study parallel the altered phenotype for body size as those in the Dutch famine studies and rodent experiments showing DNA hypomethylation associated with maternal nutrient restriction during pregnancy and the epigenome of exposed offspring (Burdge et al., 2007; Burdge & Lillycrop, 2010). In summary, exposure to chronic nutritional deprivation during the critical period for long bone formation (second trimester) was associated with reduced child height postnatal. Catchup growth apparently did not occur.

The results of this study are highly suggestive but not definitive, for several reasons. First is the lack of an indicator of measurement reliability. Second, the absence of information on leg length, a consistent measure of nutritionally sensitive growth at early ages (Frisancho, 2007; Karlberg, 1989; J. M. Tanner, Hayashi, Preece, & Cameron, 1982; Whitley, Smith, & Vaillancourt, 2013) is a limitation of the present study. Third, if exposure to Ramadan impacts survival, the measured associations are downward biased. One study, which did not include data from Iran, did not find a significant effect of prenatal exposure to Ramadan and neonatal mortality (Karimi, 2017). In addition, a more comprehensive approach will consider information on maternal body composition before and after Ramadan and ethnographic data on mothers' behavior during the observance of Ramadan fasting. The later may explain women's decision whether or not to observe fasting. Therefore, the findings of this study need to be confirmed by future studies using larger datasets and height measures that include inter- and intra-observer measurement error. These results should be used for more informed policy-making aimed at the protection and support of pregnant women. These results suggest that exposure to Ramadan (either directly through maternal fasting or indirectly via community-level fasting) is a nutritional shock to the developing fetus, indicated by decreases in height, significant in males but only a non-significant trend in females. These findings raise the question of whether and how public policy can protect and support those with underlying health problems, indicated by height, and have limited ability to respond to commonly used economic stimulators such as tax deductions and conditional cash transfers (Mankiw & Weinzierl, 2010).

Ramadan-induced nutritional stress is directly related to individual gravida's fasting decisions. Islam exempts pregnant women from fasting during Ramadan because of its potential adverse effects on health. Nevertheless, in most Muslim countries, many pregnant women fast during Ramadan because they are unaware of the exemption (Joosoph, Abu, & Yu, 2004; Mubeen, Mansoor, Hussain, & Qadir, 2012; van Bilsen et al., 2016). Lack of awareness of the exemption from Ramadan fasting among Iranian women is not higher than that in other Muslim countries. Most pregnant Iranian women who fast believe that their fasting is "recommended," *mostahab*, in Islam. Reluctance to make up for missed fasting days after pregnancy is another reason for fasting among pregnant Iranian women (Firouzbakht, Nikpour, Salmalian, Ledari, & Khafri, 2013). Therefore, a potential policy may aim at providing information about the exemption from fasting for pregnant women.

5 | CONCLUSION

The association between prenatal (second trimester) exposure to Ramadan and reduced child height is an important predictor of long-term health. However, these results need to be interpreted carefully because of (a) sample size limitation and (b) lack of measurement reliability for height. The ideal analysis of height requires a large number of individuals at each age, including (a) replicate measurements of every tenth individual, and (b) maternal behavior during pregnancy (eg, smoking, physical labor, antenatal care, and fasting). Future research should also analyze the association of prenatal exposure to Ramadan fasting with birth weight in Muslim countries. Such research is feasible because several countries (ie, Iran, Saudi Arabia, Turkey, United Arab Emirates) have comprehensive birth and death registries and vital statistics systems that have been operating for more than a decade.

AUTHOR CONTRIBUTIONS

Seyed M. Karimi: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing-original draft; writing-review and editing. **Bert Little:** Conceptualization; formal analysis; investigation; methodology; project administration; validation; visualization; writing-review and editing. **Mohammadali Mokhtari:** Data curation; formal analysis; investigation; methodology; project administration; software; writing-original draft; writing-review and editing.

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TABLE A1 Characteristics of parents and households by the accuracy of reporting children height

		Inaccurate height	Accurate height
N		15 523	5745
Mother's height (cm)		161.6	161.5
SD		10.3	9.3
Father's height (cm)		172.1	172.2
SD		11.6	9.9
Mother's age (year)		37.0	38.4
SD		8.2	8.3
Father's age (year)		42.4	44.0
SD		9.0	9.1
Mother's Edu	Illiterate	3.5%	4.2%
	Some primary sch.	7.4%	7.3%
	Some middle sch.	14.4%	14.0%
	Some high sch.	16.3%	16.4%
	High sch. Diploma	39.2%	37.7%
	Associate	6.5%	6.1%
	Bachelor	11.0%	12.2%
	Graduate sch.	1.6%	2.1%
Father's Edu	Illiterate	3.7%	4.1%
	Some primary sch.	8.1%	8.1%
	Some middle sch.	16.1%	15.8%
	Some high sch.	16.2%	15.3%
	High sch. Diploma	31.5%	31.8%
	Associate	7.3%	7.0%
	Bachelor	12.3%	12.5%
	Graduate sch.	4.8%	5.4%
Ownership of Residence	Own	54.9%	57.5%
	Rent	45.1%	42.5%
Area of residence (m^2)		90.2	92.7
SD		74.2	74.3

Source: Tehran Urban HEART 2011, Municipality of Tehran.

TABLE A2 The effect of exposure to Ramadan during the trimesters of gestation on a child's parental and household characteristics

Measure of exposure	Father's height (cm)	Mother's height (cm)	Father's age (years)	Mother's age (years)	If father is college educated (%)	If mother is college educated (%)	If household owns the residence (%)	Area of the residence (m^2)	If household lives in a low-income district (%)	If household lives in a middle-income district (%)	If household lives in a high-income district (%)
N	4931	4931	4931	4931	4931	4931	4931	4931	4931	4931	4931
Exposed in	−0.39	−0.12	−0.15	0.04	−0.9	2.4**	−3.7**	−1.9	0.2	−1.2	1.0
trimester 1	(−1.05, 0.27)	(−0.73, 0.48)	(−0.52, 0.23)	(−0.30, 0.39)	(−3.5, 1.8)	(−0.0, 4.9)	(−7.2, −0.2)	(−6.7, 2.9)	(−2.8, 3.2)	(−4.8, 2.5)	(−1.6, 3.6)
Exposed in	−0.00	−0.05	−0.17	0.01	1.0	−2.4**	−0.7	−0.6	−1.9	−0.5	1.2
trimester 2	(−0.62, 0.62)	(−0.61, 0.52)	(−0.52, 0.18)	(−0.32, 0.33)	(−1.5, 3.5)	(−4.7, −0.1)	(−3.9, 2.6)	(−5.1, 3.8)	(−4.7, 0.9)	(−3.9, 2.9)	(−1.3, 3.6)
Exposed in	−0.08	0.12	−0.01	0.01	−0.3	−1.1	1.0	−0.3	−0.7	−0.2	0.2
trimester 3	(−0.76, 0.59)	(−0.49, 0.74)	(−0.39, 0.37)	(−0.35, 0.36)	(−3.0, 2.4)	(−3.6, 1.4)	(−2.6, 4.5)	(−5.1, 3.8)	(−3.7, 2.4)	(−3.9, 3.5)	(−2.4, 2.9)

Note: Each set of coefficients in a column is the result of a separate regression. A regression's left-hand-side variable is the control variable of interest, specified in the top row of the column. Its right-hand-side variables are dummies that indicate exposure during trimesters of gestation and the rest of the control variables. Therefore, each entry of the table is the effect of exposure to Ramadan during the corresponding episode of gestation on an individual's parental and household characteristics, controlled for their other characteristics. When a binary variable was used in the left-hand-side of a regression, the estimated coefficients were multiplied by 100 to represent the effect of exposure to Ramadan on the likelihood of state (for example, the individuals having a college-educated mother) in percentage points. SEs were clustered at the city district level. Numbers in parentheses represent 95% confidence intervals.

Source: (*Data*) Tehran Urban HEART 2011, Municipality of Tehran.

**Indicate the statistical significance level at the 5%.

TABLE A3 Number of Tehrani households in HEIS during 1998 to 2011

Year	Frequency	Percent
1998	1723	9.7
1999	1779	10.0
2000	1564	8.8
2001	1559	8.8
2002	1555	8.8
2003	1180	6.6
2004	1184	6.7
2005	1185	6.7
2006	1185	6.7
2007	1185	6.7
2008	1095	6.2
2009	461	2.6
2010	1004	5.7
2011	1099	6.2
Total	17 758	100.0

Note: Authors' calculations.
Source: Iran's Household Expenditure and Income Survey (HEIS).

TABLE A4 Number of urban households in HEIS during 1998–2011

Year	Frequency	Percent
1998	8285	4.1
1999	12 731	6.3
2000	12 320	6.1
2001	12 337	6.1
2002	15 114	7.5
2003	10 959	5.5
2004	11 625	5.8
2005	12 925	6.4
2006	14 175	7.1
2007	15 018	7.5
2008	19 381	9.6
2009	18 664	9.3
2010	18 701	9.3
2011	18 727	9.3
Total	200 962	100.0

Note: Authors' calculations.
Source: Iran's Household Expenditure and Income Survey (HEIS).

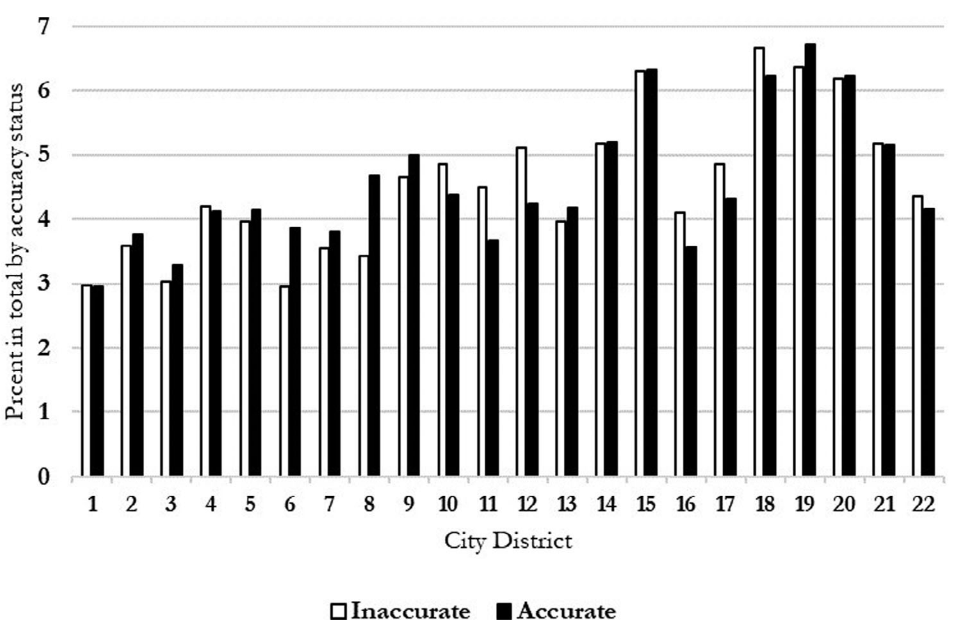

FIGURE A1 Distribution of children across city districts by the accuracy of height reporting (%). *Note*: In the figure, a white (black) column indicates the share of children with inaccurate (accurate) height in the corresponding district in total number of children with inaccurate (accurate) height. *Source*: (*Data*) Tehran Urban HEART 2011, Municipality of Tehran

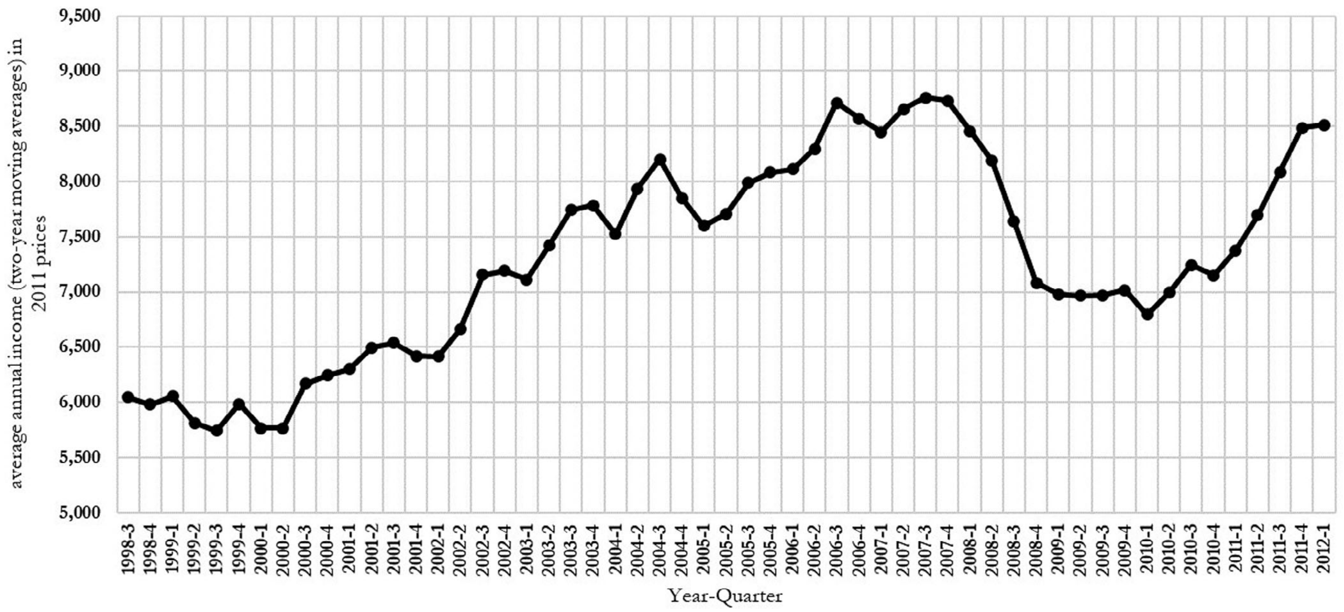

FIGURE A2 Iranian urban household's average annual income (two-year moving averages) in 2011 prices by season of interview, values in 1000 Iranian toman (TIT)—about 1.2 USD in 2011. *Note*: Authors' calculations. *Source*: Iran's Household Expenditure and Income Survey (HEIS), 1998–2011

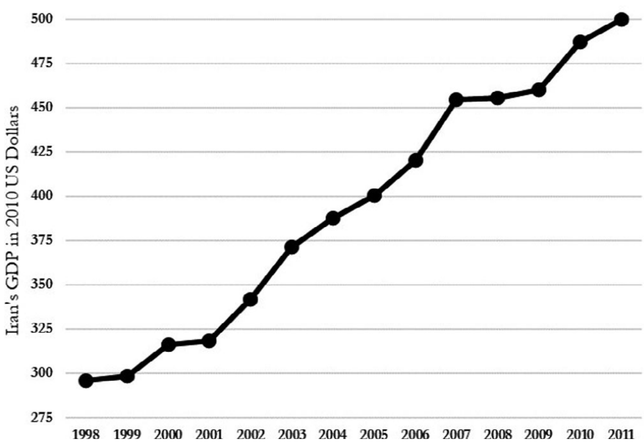

FIGURE A3 Iran's gross domestic product (GDP) in 2010 USD, values in billion dollars. *Source:* The World Bank Data Bank (https://data.worldbank.org/indicator/NY.GDP.MKTP.KD?end=2012&locations=IR&start=1998)

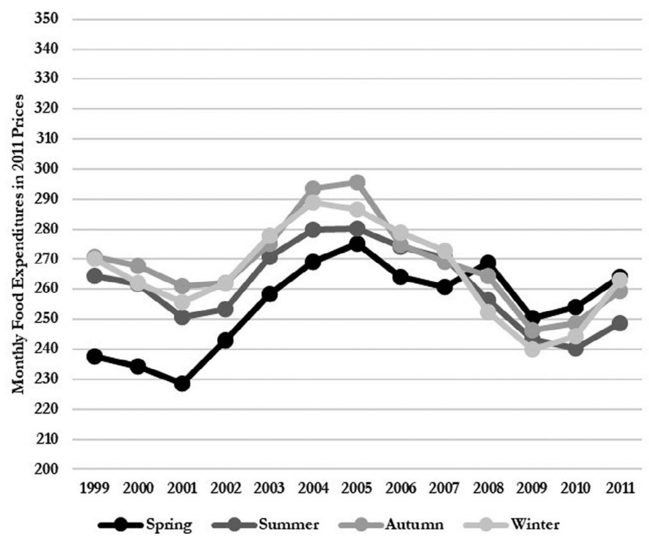

FIGURE A4 Iranian urban household's total monthly food expenditures (two-year moving averages) in 2011 prices by season of interview, values in 1000 Iranian toman (TIT)—about 1.2 USD in 2011. *Note*: Authors' calculations. *Source*: Iran's Household Expenditure and Income Survey (HEIS), 1998 to 2011