

The Effect of Ramadan Fasting on Thyroid Hormones in 9-13 Years Old Pre-Menarche Girls

Shohereh Bahrayni¹, Rahim Vakili^{2*}, Mohsen Nematy³, Abdolreza Norouzy⁴, Seyed Isaac Hashemy⁵, Mehdi Ebrahimi¹, Elham Masoumi¹, Habibolla Esmaeili⁶

¹ Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

² Emam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

³ Biochemistry and Nutrition, Endoscopic & Minimally Invasive Surgery, and Cancer Research Centers, Department of Nutrition, Mashhad Medical School, Mashhad University of Medical Science, Iran

⁴ Nutrition and Biochemistry Research Center and Department of Nutrition, Mashhad Medical School, Mashhad University of Medical Science, Iran

⁵ Addiction Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

⁶ Department of Statistic, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran

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ABSTRACT

Introduction: Muslims fast from dawn to dusk during Ramadan. The effects of prolonged food deprivation on endocrine hormones have been studied in healthy adults but no previous study has investigated this effect on children. This study aimed to evaluate the feasible changes in serum level of thyroxin (T3), tetraiodothyronin (T4), thyroid stimulating hormone (TSH) and body composition in pre-menarche girls.

Methods: This cohort study was performed through Ramadan 2012. We enrolled fifty-eight 9-13 years old girls (weight 34.20 ± 7.96 kg, height 142.01 ± 7.76 cm) in two groups from (31 and 27 in fasted and non-fasted groups, respectively) prior to Ramadan until afterwards. Weight and height of the subjects were measured using standard methods, and then Body Mass Index (BMI) was calculated. Body composition was measured using Bio Impedance Analyzer (BIA) method. Serum concentrations of T3, T4 and TSH hormones were measured by Radio Immunoassay (RIA).

Paired t-test was used to compare result of each group before and after Ramadan. Independent t-test was used to compare two groups together. Tanner intervention variable was controlled by generalized linear models intervening test. SPSS.11 software was used for data analysis.

Results: Ramadan fasting induces a significant decrease in BMI and weight on fasted group ($P=0.005$, $P=0.044$, respectively) while a significant increase was observed in non-fasted group ($P<0.001$). Although, T3 decreased significantly by fasting ($P<0.001$), it remained in the normal range. Hence, T4 decreased and TSH increased slightly in both groups.

Conclusions: According to our findings, despite a significant reduction of T3 in fasting group, variation in thyroid hormones level remained in the normal range during Ramadan fasting.

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Introduction

Many famous religions around the world recommend a period of fasting per year. During the month of Ramadan, Muslims are expected to fast due to Islamic beliefs; they refuse food and fluid from just before sunrise to sunset each

day for one month (1, 2). The exact dates of Ramadan change every year because Islam uses a lunar calendar. So as the lunar months are shorter than the solar months used elsewhere, Ramadan begin on different times each year,

* Corresponding author: Rahim Vakili, Emam Reza Hospital, P.O. Box: 91735, Mashhad, Iran. Fax: +98 511 8593038, E-mail: vakilir@mums.ac.ir

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Subsequently length of the fast is not fixed and varies based on the season that the month is placed in it and the geographical location, and the duration of fasting varies from 12 to 19 hours per day (3).

Through Ramadan, the majority of Muslims eat two principal meals; one before dawn (Sahari) and another immediately after sunset (Iftar). Islamic fasting is a Special model of fasting for one month (4). Hence, this model of fasting may causes metabolic and hormonal changes in the body that would be different from a regular fasting (5).

Islamic fasting as a compulsory law for Muslim girls must be started since the age of nine years old if they are in full health. However, there are few studies about fasting effects on thyroid hormones in adult. Studies about impact of Ramadan fasting on physiological and hormonal systems are limited. Many parents have concerns about the long-term effects of Ramadan fasting on their daughters' growth particularly due to start of puberty in these years.

To our knowledge there is no study about the hormonal changes in fasted children especially girls. The main purpose of this study was to determine the effects of Ramadan fasting on the thyroid hormones in 9-13 years girls. We designed this study to compare the effect of Ramadan fasting on the thyroid hormone profile in fasted girls compared with a group of non-fasted girls.

Methods

Study design

This prospective study was performed during Ramadan of 1433 A.H (between July to August 2012) in Mashhad, Iran. Participants were selected from families affiliated with Emdad Imam Khomeini charity. Then, based on the willingness of the participants, they were divided into two groups, the fasting and non-fasting. Tanner stages of the participants were determined by the endocrine pediatrician based on clinical examination.

Study population

Fifty eight girls aged 9 -13 years were selected among those living in city of Mashhad in north east of Iran.

Sample size

As this was a pilot study the sample size for each group was 30 persons. The participants were divided into two groups. Eventually 58 participants completed the study (31 on Fasted and 27 non-fasted).

Inclusion and exclusion Criteria

STROBE 2007 (v4) checklist was used for this study. Inclusion criteria included: The girls 9-13 years aged living in Mashhad, the tendency to contribute to the project (recorded by informed consent form), absence of menarche (menarche diagnosis was based on clinical history) and acceptance of the study requirements (fasting for at least 20 days for fasting group, 8 hours sleep, moderate activity, isocaloric diet). Exclusion criteria included: Any autoimmune disorder, cardiac or renal disease, chronic inflammation, thyroid disease, diabetes mellitus and children on special diets.

Questionnaire

Demographic factors such as: Age, education, number of fasting days past medical history were all accessed and recorded through interview with the participants and their mothers.

Anthropometric measurements

Height were, recorded by a standard clinical stadiometer with an accuracy of ± 0.01 cm. Weight was measured with light clothes and without shoes by bio impedance analyzer (BIA), BC-418 MA model.

Blood sampling and laboratory

After 12 h fasting, 5 CC blood sample was obtained for measurement of T3, T4 and TSH, Three days before Ramadan and then a day afterwards. Collected The sera was separated thirty minutes after sampling, by centrifuge (3-30K, Sigma, Germany) at 3000 rpm in 4 ° C for 10 minutes. Then the sera were collected into sterile micro tubes. After labeling, the samples were stored at - 80 ° C in the central laboratory of Mashhad University of Medical Sciences until the second sampling procedure. Serum TSH concentrations were measured with Radio Immunoassay (RIA) method and Diasource company kits (KIP1891:96). To measure serum T3 and T4 concentrations RIA and RADIM SPA

company kits (00040-125, Italy) were used.

Ethical considerations

The study aims and methods were explained to the participant and the signed informed consent forms were obtained from them prior to participation. Besides, the study protocol was approved by Ethical Committee in Research of Mashhad University of Medical Sciences.

Statistical Analysis

After collection, coding and entering data into the computer, SPSS.11 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Kolmogorov-Smirnov test was used to assess the distribution of the variables. Parametric tests were used for normally distributed data. Chi-square test was used to check the homogeneity of qualitative variables in two groups. Paired t-test was used to compare before and after measures in each group. Independent t-test was used to compare groups together by. Tanner intervention variable was controlled by using generalized linear models intervening test. The results of the data were reported as mean \pm standard deviation. The significance level was set at P-value less than 0.05.

Results

Sixty-five healthy volunteers (9-13 years girls) participated in this study, thirty four volunteers on non-fasted group and 31 participants on fasted group. Finally fifty eight subjects completed the study. Three persons were excluded from the fasting group (one because menarche issue and two because they fasted less than 20 days). Four persons were excluded from the non-fasted group (one due to menarche issue and two ones due to departure from the city of study and another one denied to continue the study). Fifty eight remaining participants were followed during the period of the study until the end of Ramadan. The mean age of the participants in the fasting and non-fasting groups was 11.06 ± 1.15 and 10.88 ± 1.31 years, respectively (range: 9-13 years). The baseline characteristics of the participants are shown in Table 1. The distribution of tanner stages at baseline in two groups is shown in table 2.

The mean and standard deviation of weight, BMI, TSH, T3 and T4 in the two groups before and after Ramadan is shown in Table-3. As is demonstrated in this table the weight has been reduced significantly in the fasted group after Ramadan ($P=0.04$), while in the non-fasted

Table1. Demographics of 58 participants

Variable	Fasting	Non-fasting	Total	T-test results
	Mean \pm SD	Mean \pm SD	Mean \pm SD	
Age(year)	11.06 ± 1.15	10.88 ± 1.31	10.97 ± 1.22	P-value =0.58
Height(cm)	143.16 ± 7.44	140.70 ± 8.06	142.01 ± 7.76	P-value =0.23
Weight(kg)	35.57 ± 7.99	32.61 ± 7.76	34.20 ± 7.96	P-value =0.16
BMI*(kg/m ²)	17.20 ± 2.85	16.26 ± 2.48	16.76 ± 2.70	P-value =0.19

*BMI: body mass index

Table2. Distribution of Tanner stages at baseline in two groups

Variable	Fasting		Non-fasting		Total	
	Number	Percent	Number	Percent	Number	Percent
Taner1	5	16.1	9	33.3	14	24.1
Taner2	12	38.7	10	37.0	22	37.9
Taner3	14	45.2	8	29.6	22	37.9
Total	31	100.0	27	100.0	58	100.0
Chi-square test	$\chi^2 = 2.69$				P-value = 0.25	

Taner1: The first stage of breast development (before breast growth)

Taner2: The second stage of breast development

Taner3: The third stage of breast development

group weight was significantly increased ($P<0.001$). And the changes in weight before and after fasting were significantly different between the groups ($P<0.001$). Hence, the mean weight reduction in the fasting group was 330 gr while it increased up to 990 gr in non-fasting group. Also, by controlling the confounding variable tanner stage, changes in body weight was significantly different between the two groups ($f=38.921$, $P<0.000$), but there was no Correlation between tanner stage and fasting ($f=2.133$, $P=0.129$).

In the subjects, BMI significantly decreased after Ramadan in the fasted group ($P=0.005$). And in the non-fasted group increased significantly ($P<0.001$). Also the difference between two groups was statistically significant ($P<0.001$). Moreover, with control of confounding variable of tanner stage, BMI was significantly different between two groups ($f=36.485$, $P=0.000$), but there was no correlation between tanner stage and fasting ($f=2.178$, $P=0.123$).

Changes in serum TSH levels before and after Ramadan, despite an increase in both groups

was not statistically significant and also the changes in serum TSH levels before and after Ramadan were not significantly different between two groups. Besides When the tanner stage variable is controlled as a confounding variable, TSH changes was not significantly different between two groups ($f=0.87$, $P=0.769$), but there was no correlation between the tanner stage and fasting ($f=0.310$, $P=0.735$).

T3 hormone levels were dramatically decreased in both groups after Ramadan. The changes in serum T3 levels before and after Ramadan were not significant different between two groups. By controlling the confounding effect of Tanner stage, T3 was not dramatically different between two groups ($f=2.918$, $P=0.094$) and there was no correlation between tanner stage and fasting ($f=0.357$, $P=0.701$).

Ser T4 levels before and after Ramadan, despite decline in both groups was not statistically significant. By controlling the tanner stage, T4 levels were not significantly different between two groups ($f=0.193$, $P=0.662$) and there was no correlation between tanner stage and fasting ($f=0.066$, $P=0.936$).

Table3. The mean and standard deviation of weight (kg), BMI(kg/(m)²), TSH(mIU/ml),T3(ng/dl) and T4(μg/dl) in the two groups before and after Ramadan

Variable Groups	Before Ramadan		After Ramadan		The difference before and after	Paired t-test results	
	P	t	P	t		P	t
Weight(kg): Fasting	35.57 ± 7.99		35.24 ± 7.75		-0.32 ± 0.87	0.04*	2.1
Non-fasting	32.61 ± 7.76		33.60 ± 7.61		0.98 ± 0.66	< 0.001*	-7.70
T-test results	0.16	1.42	0.42	0.81	< 0.001*	-6.38	
BMI(kg/m²): Fasting	17.20 ± 2.85		16.98 ± 2.71		-0.21 ± 0.40	0.005*	3.00
Non-fasting	16.26 ± 2.48		16.67 ± 2.37		0.40 ± 0.36	< 0.001*	-6.20
T-test results	0.19	1.32	0.64	0.45	< 0.001*	2.60	
TSH(U/mlμ): Fasting	4.32 ± 1.55		4.65 ± 1.67		0.32 ± 1.32	0.18	-1.37
Non-fasting	3.98 ± 1.64		4.14 ± 1.63		0.16 ± 1.67	0.61	-0.50
T-test results	0.41	0.82	0.24	1.17	0.68	0.41	
T3(ng/dl): Fasting	193.83 ± 21.46		169.77 ± 18.04		-24.06 ± 17.92	< 0.001*	7.47
Non-fasting	190.33 ± 28.54		180.81 ± 19.81		-9.51 ± 34.47	0.163	1.43
T-test results	0.59	0.53	0.03	-2.22	0.056	-1.97	
T4(μg/dl): Fasting	9.64 ± 1.73		9.63 ± 2.71		-0.009 ± 2.00	0.97	0.02
Non-fasting	10.14 ± 1.66		9.95 ± 1.93		-0.192 ± 2.05	0.63	0.47
T-test results	0.27	-1.11	0.61	-0.50	0.73	0.34	

BMI: body mass index

TSH: thyroid stimulating hormone

T3: thyroxine

T4: tetra-iodo thyronin

*: Significant P

Discussion

Islamic law expect fasting for women to start at age of 9 (according to some clergy mans). They must refuse drinking and eating from sunrise until sunset while they can eat during other hours. This lifestyle can have some metabolic and hormonal effects on the body (5). Normal growth in childhood depends on adequate nutrition, proper mental environment, lack of disease and the secretion the sufficient amounts of metabolic hormones (6). The essential role of the thyroid hormones for normal puberty and sexual development is well known (7).

The previous studies have showed weight loss throughout Ramadan month (8, 9). In contrast to this, one study reported weight gain during Ramadan fasting (10) and some others did not find any significant change in weight (11, 12). A study showed dramatic reduction of BMI and weight during Ramadan compared with before (13). Study of Azizi and his colleagues showed that fasting reduced BMI, but it had no considerable effect on leptin and adiponectin levels (14).

Our study indicated that weight and BMI noticeably decreased during fasting. The previous studies had no control group but the findings of our study showed that weight and BMI in the non-fasting group increased significantly after Ramadan.

Coiro showed that fasting is associated with a dulled TSH response to TRH, but basal TSH and thyroid hormone levels remain within the normal range (15). Bogdan reported a flattened circadian rhythm for serum TSH during Ramadan fasting (16), but Sajedi indicated a significant steady increment of TSH throughout this month (17). Our finding in this study showed that TSH increased slightly in both groups but not significantly. Studies have showed that long-term experimented fasting, after 48 hours, decreased T3 but conversely response of TSH to TRH has been decreased or unaltered (18). It seems T4 decreases significantly in both gender after Ramadan but TSH might increase significantly in men (5, 19).

We found a significant reduction in T3 level after Ramadan in fasting group and decrease in T3 level in non-fasted group but it was not

significant. Also we observed an inconsiderable reduction in T4 level after Ramadan in two groups but again not significant. However, hormonal variations in our findings all were in the normal range. Chan *et al* observed that fasting induced a reduction in T3 levels by about 30% and this is due to decline in leptin level. Leptin regulates changes caused by fasting in the hypothalamic-pituitary-thyroid axis (20). Previous studies suggest that in total caloric deprivation, the serum T3 concentration rapidly declines. A period of 24 hours fasting might significantly reduce T3 while serum T4 is steady during this period. The lack of significant changes of T4 and T3 within 14 hours of fasting could be due to the long half-life of T4 and T3 (8 and 1 day, respectively). In the last days of Ramadan, T4 and T3 levels dropped in women, that may be due to reduction of the total concentration of protein binding, while the free hormones index remained normal (21). A little but significant increase in serum T4 in the last days of Ramadan has been reported by some studies (14) but not confirmed in the others (11, 13 and 18). More than 99% of T3 and T4 are immediately bound to the blood with several plasma proteins after secretion into blood. These hormones are bound mainly with thyroxin binding globulin (TBG) and less with albumin and pre-albumin (22-24).

It has been shown that reduction of T4 and T3 levels is mainly due to alteration in TBG (25). It has reported that no significant alterations in serum concentration of T4, T3, TSH, and TSH take part in response to intravenous injection of TRH occurs in male subjects during Ramadan (26).

The length of Ramadan fasting is not enough to cause any steady alteration in the pituitary-thyroid axis or peripheral conversion of T4 (27). Difference in the effects of fasting on thyroid hormones levels in some published studies perhaps is due to change in the diet in month of Ramadan, effect of circadian rhythm and the number of fasting days.

Limitations

This study studied the healthy girls and it is not representative for thyroid disease patients. This study was performed on a particular population (people supported by the Emdad

Imam Khomeini charity). It is suggested to do a study on various population groups.

Strengths

According to our knowledge, we examined the effect of fasting on 9-13 years girls for the first time. In our study, we included a control group while the previous studies only enrolled a single group of fasting adults.

Suggestions

We suggest that study be done with larger sample sizes and separately in various pubertal stages. Also it is recommended to do study on the boys in pubertal age.

Conclusions

This study demonstrated that Ramadan fasting significantly decreased T3 level but within the normal range. Moreover, the results of this study showed that TSH and T4 did not changed by Ramadan Fasting. Finally the findings demonstrated fasting has no negative effect on thyroid hormones in 9-13 years healthy girls before the age of menarche.

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