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Effect of fasting during Ramadan on fetal development and maternal health

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Abstract

Aim: The aim of the present study was to determine whether fasting during Ramadan causes ketonemia and/or ketonuria and their effects on fetal intrauterine development.

Methods: Thirty-six consecutive healthy women with uncomplicated pregnancies of ≥20 weeks of gestation who were fasting during Ramadan were included in the study group (group 1). The control group (group 2) consisted of 29 healthy pregnant women who were not fasting. Doppler ultrasonography was performed in all subjects in the beginning and at the end of Ramadan to evaluate the changes in the following measurements: fetal biparietal diameter; fetal femur length; and estimated fetal body weight. Fetal biophysical profile, amniotic fluid index, and umbilical artery systole/diastole ratio were measured in the beginning and at the end of Ramadan. Effects of fasting on the mother were evaluated by measuring serum concentrations of 3ß hydroxybutyrate and glucose, and urinary concentration of ketone. Subjects with any of the followings were excluded: diabetes; thyroid dysfunction; Cushing's syndrome; adrenal disease; preeclampsia; and multiple pregnancy.

Results: The mean duration of fasting in the study group was 18 ± 2.1 days. The mean maternal glucose level was significantly lower in the study group than in the control group ($P = 0.003$). No statistically significant differences were found between the two groups in the comparisons of other parameters.

Conclusion: We concluded that fasting during Ramadan does not lead to maternal ketonemia or ketonuria in pregnant women. In addition, fasting during Ramadan has no significant adverse effect on intrauterine fetal development or the fetus's health.

Key words: fasting, fetal development, ketonemia, ketonuria, Ramadan.

Introduction

Ramadan is a period during which food and fluid ingestion is not allowed for Muslims between pre-sunrise and post-sunset hours for one month every year. The metabolic adaptation in humans to starvation and carbohydrate restriction is a complex process and involves a number of hormones, substrates, and tissues.[1–3] The need for ketoacids, beta-hydroxybutyric acid, and acetoacetic acid to replace glucose as the primary fuel for brain of a fasting man appears to be the key to maximum protein conservation.[1–3] Urinary loss of ketoacids (ketonuria) occurs in starving subjects (100–150 mM/day or 40–60 calories/day).[4] It is also known that mild ketosis may occur in the mother and fetus during the third trimester, and in the newborn infant in the early neonatal period.[5] The effects of fasting on pregnancy have been investigated by several authors previously.[3,6] However, ketonemia and/or ketonuria in pregnant women fasting during Ramadan have never been studied before.

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The present study was designed to investigate whether fasting during Ramadan causes ketonemia, and/or ketonuria in pregnant women and their effects on fetal intrauterine development.

Methods

This prospective study was conducted in the Obstetrics and Gynecology Department of Gaziantep University Hospital between September 23 and October 23 in 2006 (during the month of Ramadan). Consecutive healthy women with singleton uncomplicated pregnancies of ≥20 weeks of gestation were enrolled in to the study if they signed an informed consent. Subjects who were fasting during Ramadan were included in group 1, while those who were not fasting were included in group 2 as a control group. The study protocol was approved by the local institutional ethics committee.

All of the subjects were examined by Doppler ultrasonography in the beginning and at the end of Ramadan for the evaluation of any changes in the following measurements: fetal biparietal diameter (BPD); fetal femur length (FL); estimated fetal body weight (EFBW); fetal biophysical profile (BPP); amniotic fluid index (AFI); and umbilical artery systole/diastole (S/D) ratio. High definition image (HDI; A 3.5 MHz convex transducer, Applio-Toshiba, Otamara, Japan) was used to obtain AFI and Doppler waveforms.

The modified biophysical profile was scored according to Manning criteria as follows:[6]

- *Fetal movements:* three or more body or limb movements within 30 minutes.
- *Fetal tone:* one episode of active extension and flexion of the limbs; opening and closing of hand within 30 min.
- *Fetal breathing movements:* one or more episode greater than 30 seconds within 30 min (hiccups are considered breath activity).
- *Amniotic fluid volume*: a single 2 × 2 cm pocket is considered adequate.

The total score for the above biophysical profile was 8. For each variable, a score of 2/2 was given if it fulfilled criteria, a score of 0/2 was recorded if the criteria were not met in less than 30 min; no further biophysical assessment was needed.

Amniotic fluid index was also calculated by the sum of the deepest vertical pocket in four uterine quadrants measured by sonography.[7,8] Oligohydramnios is defined as an amniotic fluid index of ≤5 cm. To remove the effect of other factors causing oligohydramnios and polihydramnios, all cases with urinary or skeletal anomalies, intrauterine growth retardation, multiple pregnancy, diaphragmatic hernia, diabetes, fetal hydrops and premature rupture of membranes were excluded from the study.

Umbilical artery systole/diastole ratio was calculated as follows: during Doppler ultrasonography, the wall filter and sample gate were set at 100 MHz and 2 mm, respectively. Umbilical artery Doppler velocimetry was performed with a sample gate placed at the umbilical artery near the placental insertion site. Uterine artery waveforms were measured from both sides of the uterus while the patient was in a semi-recumbent position, and the transducers were placed in a longitudinal plane along the inguinal area. Color Doppler imaging was used to target the uterine artery at the site of overlap with external iliac artery. The quality of the flow velocity waveforms was maximized by using the smallest possible angle of insonation and acceptance of only those with sharp and definite outline. When ≥5 consecutive uniform waveforms were obtained, the image was frozen and waveform evaluation was performed. Peak systolic (S) and diastolic (D) velocity was measured to calculate S/D ratio. Abnormal umbilical artery Doppler velocimetry was defined as S/D ≥ 3.0 or presence of absent or reversed of end diastolic flow, whereas abnormal uterine artery Doppler velocimetry was defined as S/D ≥ 2.6 or presence of early diastolic notch in either side of the uterus.[8] Abnormal Doppler velocimetry per se was not considered as an indication for cesarean section.

Maternal effects of fasting during Ramadan were assessed by measuring blood concentration of glucose, 3ß hydroxybutyrate, and urinary ketone levels. Maternal blood for the above measurements were taken at 6:30 PM (right before subjects are allowed to eat) during weekly routine controls.

3ß hydroxybutyrate concentrations were measured by capillary test (Optimum Betaketone test strips; Medisense, Abingdon, Oxon UK) to show ketosis. Ketonuria was measured by urine analysis strips (Invitro diagnosticum urinanalysis labstrip; Roche Diagnostics GmbH, Mannheim, Germany). Maternal blood glucose levels were measured using a glucometer (Accu-Check Active; Roche Diagnostics).

Multivitamin (Materna Tablets, Wyeth Pharmacy, Turkey), calcium (1 g/day) and iron (100 mg/day) supplementation were given to all subjects. All of the subjects were advised to drink at least 2 L of water every night to prevent hypo-hydration.

Table 1 Comparison of the maternal data between group 1 (fasting) and group 2 (non-fasting)

Variable	Group 1 ($n = 36$)	Group 2 ($n = 29$)	*P*-value
Age (years)†	24 (5.3)	26 (4.2)	0.176
Parity‡	2 (1–2.25)	2 (1–2.25)	0.943
Gestational age (week)†	28.5 (3.9)	30.6 (3.4)	0.207
Time relapse for oral intake (h)‡	13 (12–14)	2 (1.75–2.25)	0.001
Maternal glucose level (mg/dL)‡	67 (66–78.5)	90 (80–91.2)	0.003
Maternal weight gain (kg)‡	1.0 (1–1.2)	1.0 (1–1.5)	1.000
Maternal blood ketone level (μmol/L)‡	1 (0–1)	0 (0–1)	0.419
Urine ketone level (μmol/L/L)	1 (0–1)	0 (0–0.2)	0.12

†Data is given as mean (SD); ‡data is given as median (25%–75%).

Table 2 Comparison of the fetal data between group 1 (fasting) and group 2 (non-fasting)

Variables	Group 1	Group 2	*P*-value
Increase in fetal BPD (mm)	4.5 (3.7–5.8)	4.0 (3.1–5.2)	0.621
Increase in fetal FL (mm)	3.2 (2.6–3.8)	3.0 (2.7–3.4)	0.542
Increase in EFBW (g)	221 (200–357)	214 (229–340)	0.219
Umbilical artery S/D ratio	2.7 (2.0–3.1)	2.5 (2.3–3.4)	0.315
AFİ (mm)	12.9 (12.1–14.0)	13.3 (12.5–14.6)	0.434
BPP	7.0 (6.7–8.0)	7.8 (6.9–8.0)	0.326

Data is given as mean (SD). AFI, amniotic fluid index; BPD, biparietal diameter; BPP, biophysical profile; EFBW, estimated fetal body weight; FL, femur length; S/D, systole/diastole.

Subjects with the following were excluded: diabetes; thyroid dysfunction; Cushing's syndrome; adrenal disease; pre-eclampsia; and multiple pregnancy.

Statistical analysis

Collected data were subjected to statistical analysis using Stigma Stat 3.0 (San Rafael, CA, USA). The *t*-test or Mann–Whitney Rank Sum test were used to evaluate statistical significance of differences between the two groups. A *P*-value of <0.05 was considered to be significant.

Results

A total of 65 pregnant women; 36 in the fasting group (group 1) and 29 in the non-fasting group (group 2), were studied. The mean number of fasting days was 18 ± 2.1 days. Maternal and fetal gestational age were similar in both groups.

The mean time since the last oral intake was significantly longer ($P = 0.001$), and the mean maternal glucose level was significantly lower in the study group than in the control group ($P = 0.003$).

No significant difference was observed in the comparison of the following between the two groups: mean maternal weight gain ($P = 1.000$); mean maternal ketone levels ($P = 0.419$); and mean maternal urinary ketone levels ($P = 0.12$) (Table 1).

Increases in fetal BPD, FL, and EFBW were not statistically different between the two groups ($P > 0.05$). Fetal BPP, AFI, and umbilical artery S/D ratio were within normal ranges in both groups and the difference between the groups was not significant ($P > 0.05$) (Table 2).

Discussion

The results of the present study showed that fasting during the month of Ramadan did not cause any significant untoward effects in maternal or fetal health, or in fetal development in a group of pregnant women at $\geq$20 weeks of gestation.

Ketone bodies are formed in the liver as a result of oxidation of fatty acids whenever glycogen stores are depleted.[9] The term 'ketone bodies' refers to three molecules, acetoacetate (AcAc), 3-hydroxybutyrate (3HB),

and acetone. Ketonuria reflects the passage of ketone bodies (β-hydroxybutyrate and acetoacetate) into urine as the threshold substances during maternal ketonemia.[9] Assessment of urinary ketone levels is an inexpensive test that is easily performed in an outpatient setting.[9] A transient ketonuria may occur during pregnancy as a result of a variety of maternal metabolic derangements, including dehydration, caloric restriction, and diabetic ketosis.[9] It has been shown previoulsy that ketones elicit alterations in amniotic fluid volume and composition in sheep,[10] and also elicit potentially detrimental changes in the neurologic status of animals[11] and human beings.[12] However, the results of the present study showed that fasting for about 13–14 h each day did not cause significant ketonemia in the pregnant women. On the other hand there was no difference in ketonuria levels between the fasting and non-fasting groups. We believe that giving advice to fasting group of pregnant women to drink at least 2 L of water post-sunset played an important role to prevent hypo-hydration in these subjects.

Previous studies suggested that a reduction in the body mass index of a fasting person is common; however, no evidence of an adverse effect on person's health was observed.[2,3] Similarly, Leiper *et al*. reported that Muslims undoubtedly become dehydrated during the day in Ramadan; however, the authors did not report any significant health hazard due to dehydration in those people.[13] In the present study, no difference was observed in the mean maternal weight gain of the fasting group of pregnant women compared to the non-fasting group of pregnant women. In addition, there was no significant difference in the amniotic fluid index between the two groups; this result supports the results of a previous study by Mirghani *et al*. The authors reported that maternal fasting during Ramadan caused no alterations amniotic fluid or fetal bladder volumes.[14]

Proper feeding of a pregnant woman is essential for her own health as well as that of the fetus. Recently, Kiziltan *et al*. analyzed the blood biochemical parameters of pregnant women and obtained the dietary intakes from fasting ($n = 49$) and non-fasting ($n = 49$) pregnant women.[15] In their study, weight gain and energy intake was less in the fasting group compared to the control group. Additionally, the percentage of protein and carbohydrates in total energy source was higher in the fasting group. Although the difference in total energy intake between fasting and non-fasting pregnant women was not studied, maternal weight gain was not statistically different between the fasting and the non-fasting pregnant women in the present study. Additionally, no significant difference was observed in the growth rate of fetuses between the two groups. These findings are in accordance with the findings of previous studies.[14,16] Recently, Kavehmanesh *et al*.[17] retrospectively investigated the neonates of 284 mothers with a history of Ramadan fasting during pregnancy and the neonates of 255 mothers who did not have a history of fasting during their pregnancies. They reported that maternal fasting during Ramadan did not have a significant effect on neonatal birthweight.

The effect of glucose regulation in changes of Doppler velocity waveforms has been studied mostly in diabetic pregnant women.[18] Grunewald *et al*. reported that changes in Doppler velocity waveforms are not affected by blood glucose regulation in a group of diabetic pregnant women.[18] Recently, Mirghani *et al*. showed no significant difference in umbilical artery pulsatility index between fasting and non-fasting groups of pregnant women.[14] Accordingly, no significant difference was observed in the umbilical artery systole/diastole ratio between fasting and non-fasting groups of pregnant women in the present study.

In conclusion, the results of the present study showed that fasting during the month of Ramadan did not cause any significant ketosis and/or ketonuria in pregnant women at ≥20 weeks of gestation. Additionally, no adverse effect on the course of intrauterine fetal development or maternal health was observed due to fasting during Ramadan.

References

1. Reilly T, Waterhouse J. Altered sleep-wake cycles and food intake: The Ramadan model. *Physiol Behav* 2007; **90**: 219–228.
2. Gharbi M, Akrout Mand Zouari B. Food intake during and outside Ramadan. *East Mediterr Health J* 2003; **9**: 131–140.
3. Beltaifa L, Bouguerra C, Slama B *et al*. Food intake and anthropometrical and biological parameters in adult Tunisians during fasting at Ramadan. *East Mediterr Health J* 2002; **8**: 603–611.
4. Aoki TT. Metabolic adaptations to starvation, semistarvation, and carbohydrate restriction. *Prog Clin Biol Res* 1981; **67**: 161–177.
5. Gin H, Vambergue A, Vasseur C *et al*. Blood ketone monitoring: A comparison between gestational diabetes and non-diabetic pregnant women. Blood ketone monitoring: A comparison between gestational diabetes and non-diabetic pregnant women. *Diabetes Metab* 2006; **32**: 592–597.
6. Manning FA, Morrison I, Lange I. Foetal biophysical profile scoring: A prospective study in 1,184 high-risk patients. *Am J Obstet Gynecol* 1981; **140**: 289–294.

7. Chauhan SP, Roberts WE, Martin JN Jr, Magann EF, Marrison JC. Amniotic fluid index in normal pregnancy: a longitudinal study. *J Miss State Med Assoc* 1999; **40**: 43–46.
8. Williams K, Wittman BK, Dansereuu J. Correlation of subjective assessment of amniotic fluid index. *Eur J Obstet Gynecol Reprod Biol* 1992; **46**: 1–5.
9. Onyeije CI, Divon MY. The impact of maternal ketonuria on fetal test results in the setting of postterm pregnancy. *Am J Obstet Gynecol* 2001; **184**: 713–718.
10. Ross MG, Sherman DJ, Ervin MG, Castro R, Humme J. Maternal dehydration-rehydration: Fetal plasma and urinary responses. *Am J Physiol* 1988; **255**: E674–E679.
11. Bhasin S, Shambaugh GE III. Fetal fuels. V. Ketone bodies inhibit pyrimidine biosynthesis in fetal rat brain. *Am J Physiol* 1982; **243**: E234–E239.
12. Naeye RL, Chez RA. Effects of maternal acetonuria and low pregnancy weight gain on children's psychomotor development. *Am J Obstet Gynecol* 1981; **139**: 189–193.
13. Leiper JB, Molla AM. Effects on health of fluid restriction during fasting in Ramadan. *Eur J Clin Nutr* 2003; **57**: 530–538.
14. Mirghani HM, Weerasinghe DSL, Ezimokhai M, Smith JR. The effect of maternal fasting on the fetal biophysical profile. *Int J Gynecol Obstet* 2003; **81**: 17–21.
15. Kiziltan G, Karabudak E, Tuncay G *et al*. Dietary intake and nutritional status of Turkish pregnant women during Ramadan. *Saudi Med J* 2005; **26**: 1782–1787.
16. Cross JH, Eminson J, Wharton BA. Ramadan and birth weight at full term in Asian Moslem pregnant women in Birmingham. *Arch Dis Child* 1990; **65**: 1053–1056.
17. Kavehmanesh Z, Abolghasemi H. Maternal Ramadan fasting and neonatal health. *J Perinatol* 2004; **24**: 748–750.
18. Grunewald C, Divon M, Lunell NO. Doppler velocimetry in last trimester pregnancy complicated by insulin-dependent diabetes mellitus. *Acta Obstet Gynecol Scand* 1996; **75**: 804–808.