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Effect of Ramadan Fasting on Alanine Aminotransferase (ALT) in Non-Alcoholic Fatty Liver Disease (NAFLD)

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ABSTRACT

Introduction: Effect of Ramadan fasting on non-alcoholic fatty liver disease (NAFLD) is unknown, and limited studies have been conducted in this regard. Nutritional and behavioral changes in fasting individuals during Ramadan may affect NAFLD, including a high-fat and high-calorie diet, alterations of the body weight and sleep patterns, and insufficient physical activity. The present study aimed to evaluate the effects of these changes on alanine aminotransferase (ALT), an important indicator of NAFLD deterioration.

Methods: In total, 60 patients with NAFLD were enrolled in this study and received two ALT tests before and after the holy month of Ramadan. Among the participants, 34 were fasting, and 26 cases did not fast. After data collection, subjects were divided into two groups of fasting and non-fasting and compared using the SPSS.

Results: Mean ALT changes before and after Ramadan were positively higher in the fasting group (+7.38±8.47 IU/L) compared to the non-fasting patients (-0.12±10.15 IU/L) (P=0.002), which were mostly observed in the NAFLD patients who fasted for 21-30 days.

Conclusion: According to the results, Ramadan fasting may increase the ALT level in individuals. Therefore, it is recommended that further investigations with larger sample sizes and various conditions be performed on the NAFLD patients who fast in Ramadan, focusing on the association of weight loss and education level to determine an effective dietary regimen.

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Introduction

Population of Muslims across the globe has been estimated to be 1.1-1.5 billion, comprising 18-25% of the world population. Approximately 62% of the world's Muslim population resides in Asia (1). In the holy month of Ramadan (the ninth lunar month in the Hegira calendar), Muslims fast from dawn to dusk, and in this period, they are not allowed to eat foods, drink fluids and alcohol or smoke. Length of the abstinence varies between 12-16 hours, depending on the coinciding season with Ramadan. Fasting individuals have a meal before dawn (Suhur), followed by another meal at sunset (Iftar). As an Islamic rule, it is obligatory for all healthy adult Muslims to fast in Ramadan.

Over 50% of Muslims fast every day or on some days of Ramadan (2). However, many people cannot fast due to medical conditions and diseases. Non-alcoholic fatty liver disease (NAFLD) is one of the most common diseases of the modern era. Patients with NAFLD are often concerned about the effects of Ramadan fasting on their health. If fasting is considered harmful for these patients, they must avoid fasting according to the Islamic law.

NAFLD is defined as abnormal fat accumulation in the liver cells (steatosis), in the absence of other causes. NAFLD consists of non-alcoholic fatty liver (NAFL) and non-alcoholic

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steatohepatitis (NASH). In NAFL, there is no significant hepatic inflammation, while NASH is characterized by hepatic inflammation, along with elevated plasma liver enzyme levels, such as alanine aminotransferase (ALT) and aspartate transaminase (AST), which may be histologically indistinguishable from alcoholic steatohepatitis (3).

Prevalence of NAFLD in the general population and worldwide is 6-35% (median: 25%), with the highest rate reported in industrial countries, the Middle East and South America, whereas the lowest prevalence has been reported in Africa (4, 5). Prevalence of NAFLD has increased dramatically in recent decades (6). In Iran, overall prevalence of NAFLD and mild, moderate and severe fatty liver disease has been estimated at 33.9%, 26.7%, 7.6%, and 0.5%, respectively (7). Furthermore, a lower percentage of these patients have NASH. Prevalence of NASH in Iran and other countries is approximately 3-5% (8, 9); as such, one-eighth of NAFLD patients have NASH as well.

Clinical risk factors for NASH and elevated ALT include diabetes, metabolic syndrome, and ethnicity (10). Based on these risk factors, some nutritional and behavioral changes in fasting individuals during Ramadan may affect the incidence of NAFLD, such as high-fat and high-caloric diets, alterations of the body weight and sleep patterns, and insufficient physical activity. Fasting individuals avoid eating and drinking in daytime, and many people tend to consume large meals before dawn and sunset, which often have high fat and sugar contents; such diets are likely to deteriorate NAFLD. On the other hand, fasting individuals do not smoke or drink alcoholic beverages, which are among the known risk factors for liver diseases.

Limited studies have focused on the effects of Ramadan fasting on NAFLD. In rats with Ramadan-type fasting, which were used as a model for Ramadan fasting in humans, indices of liver metabolic activities (e.g., liver lactate dehydrogenase, malate dehydrogenase, glucose-6-phosphatase, and fructose 1,6-bisphosphatase) were observed to enhance. Moreover, liver alkaline phosphatase, gamma-glutamyl transpeptidase, and leucine amino-peptidase significantly increased in the studied rats (11). In the literature search, we found no articles regarding the effect of Ramadan fasting on the liver function tests of NAFLD patients. Therefore, the present study aimed to investigate the effect of Ramadan fasting on liver function tests, particularly ALT.

Material and methods

This prospective cross-sectional study was conducted on 60 patients with NAFLD during the holy month of Ramadan (18th June-17th July 2015). Patients referring to Poursina Hakim Clinic of Isfahan city, Iran with the confirmed diagnosis of NAFLD by a gastroenterologist were selected one month prior to Ramadan. Additionally, a list of the patients with NAFLD diagnosis was prepared, whose medical records were available in the clinic. Patients were contacted by the researcher. After obtaining informed consent, baseline data of the subjects were collected, including the body weight, height, and underlying diseases (diabetes mellitus, hyperlipidemia, hypertension, and cardiovascular diseases).

Following an ALT laboratory test, a dietary regimen was prescribed for the patients (low-fat and low-calorie). After Ramadan, body weight and ALT levels were measured again in all the patients who referred to the research setting and were divided into two groups of fasting in Ramadan and non-fasting.

Data analysis was performed in SPSS version 22, using descriptive and analytical statistics, T-test, analysis of variance (ANOVA), NPar, Mann-Whitney U test, and Chi-square. In this study, P value of less than 0.05 was considered significant.

Results

In total, 60 patients completed the two follow-ups in this study, 34 and 26 of whom were categorized as the fasting and non-fasting groups, respectively. Baseline data of the NAFLD patients and matching of the study groups are presented in Table 1.

Patients were matched in terms of age, gender, education level, smoking habits, disease duration, and underlying diseases, such as diabetes mellitus, hyperlipidemia, hypertension, and cardiovascular diseases. Comparison of the fasting and non-fasting groups in terms of ALT is shown in Table 2.

According to the information in Table 2,

Table 1. Baseline Data of NAFLD Patients and Matching of Fasting and Non-Fasting Groups

Variable	Fasting (N=34)	Non-Fasting (N=26)	P-value
Age (year)	46.03±11.72	49.58±10.96	0.237
Gender			
Male N (%)	25 (73.5)	14 (53.8)	0.172
Female N (%)	9 (26.5)	12 (46.2)	
Duration of NAFLD (year)	3.90	3.55	0.150
Smoking Habits			
Yes N (%)	2 (5.8)	4 (15.4)	0.388
No N (%)	32 (94.2)	22 (84.6)	
Underlying Diseases			
Yes N (%)	13 (38.2)	7 (26.9)	0.416
No N (%)	21 (61.9)	19 (73.1)	
Dietary Regimen			
Yes N (%)	9 (26.5)	5 (20)	0.758
No N (%)	25 (73.5)	20 (80)	

Table 2. Comparison of Fasting and Non-Fasting Groups in Terms of ALT

Variable	Fasting (IU/L) Mean±SD	Non-Fasting (IU/L) Mean±SD	P-value
ALT Before Ramadan	34.64±13.51	34.94±12.23	0.930
ALT After Ramadan	42.02±17.82	34.82±15.35	0.105
ALT Changes*	7.38±8.47	-0.12±10.15	0.002#

*Mean ALT after Ramadan-mean ALT before Ramadan; #significant

fasting and non-fasting groups in the present study had no significant differences in terms of the mean ALT before and after Ramadan (P>0.05). However, mean ALT changes before and after Ramadan were positively higher in the fasting subjects (+7.38 IU/L), compared to the negative value observed in the non-fasting patients (-0.12 IU/L) (P=0.002).

According to the multiple comparison of the non-fasting group and fasting patients (length of fasting: 10-20 and 21-30 days) during Ramadan, significant differences in the mean ALT changes were only observed between the non-fasting subjects and those who fasted for 21-30 days (P=0.010). Since the length of fasting was less than 10 days in only three patients during Ramadan, these participants were not compared in this regard.

Based on the time of referral for performing the ALT test after Ramadan, the fasting patients were divided into two groups of fasting for the first 15 days of the month and 15-30 days. Compared to the patients who referred for the ALT test 15-30 days after Ramadan, patients who referred during the first 15 days after Ramadan had higher mean ALT level and ALT changes, as compared to the values obtained before Ramadan (44.21 versus 38.01, and 8.49 versus 5.76, respectively); however, the differences in this regard were not considered significant (P=0.339 and P=0.377, respectively). Comparison of the fasting and non-fasting groups in terms of body weight and body mass index (BMI) has been presented in Table 3.

Table 3. Comparison of Fasting and Non-Fasting Groups in Terms of Body Weight and BMI

Variable	Fasting (Kg-Kg/m^2) Mean±SD	Non-Fasting (Kg-Kg/m^2) Mean±SD	P-value
Body Weight Before Ramadan	88.31±19.76	83.89±10.45	0.548
Body Weight After Ramadan	87.50±18.48	83.00±10.55	0.519
Body Weight Changes*	-0.80±2.36	-0.89±2.60	0.936
BMI Before Ramadan	29.46±4.52	30.08±4.12	0.746
BMI After Ramadan	29.20±4.08	29.72±3.80	0.767
BMI Changes**	-0.26±0.74	-0.36±0.79	0.749

*Mean body weight after Ramadan-mean body weight before Ramadan; **Mean BMI after Ramadan-mean BMI before Ramadan

According to the information in Table 3, fasting and non-fasting groups had no significant differences in terms of the mean body weight and BMI before and after Ramadan, as well as the changes in these indices before and after Ramadan.

Discussion

Some of the known risk factors for developing NAFLD are metabolic syndrome (e.g., obesity, systemic hypertension, dyslipidemia, insulin resistance, or overt diabetes), male gender, old age, race/ethnicity, polycystic ovary syndrome, hypothyroidism, obstructive sleep apnea, hypopituitarism, and hypogonadism (12). Clinical risk factors for NASH and increased ALT include diabetes, metabolic syndrome, and ethnicity (10). In the current research, case and control patients were matched in terms of age, gender, smoking habits, education level, duration of fatty liver diseases, and underlying diseases, such as diabetes mellitus, hyperlipidemia, hypertension, cardiovascular diseases, and metabolic syndrome. According to our findings, these risk factors were similar between the patients in the fasting and non-fasting groups.

According to the results of the present study, Ramadan fasting increased the mean ALT level mainly in the patients who fasted for 21-30 days. It is also notable that this index continued to decline after Ramadan.

It has been established that despite the different normal ranges of various laboratories, normal serum ALT level is within the range of 29-33 IU/L in men and 19-25 IU/L in women in the absence of identifiable risk factors for liver disease (13). Patients in the present study had NAFL, which was defined as normal ALT and NASH with elevated ALT, while the mean ALT of the subjects was above the normal range before and after Ramadan. Elevation of ALT is of significance since it is an indicator of deterioration and progression of liver disease. So, Ramadan fasting can deteriorate clinical course of NAFLD. On the other hand, decreased mean ALT in the non-fasting patients could be due to the physicians' recommendations for adherence to a dietary plan and physical activity in the patients. Of note, these recommendations were also provided for the fasting patients in our study.

Fasting individuals avoid eating foods and drinking beverages during the day; however, this period of abstinence is often followed by the consumption of large meals with significant fat and sugar content at dawn and before sunset, which induces liver metabolic stress, thereby metabolizing the absorbed nutrients.

Fasting individuals have limited physical activity and altered sleep patterns and dietary regimen, but according to the current research, these nutritional and behavioral factors were not associated with significant altering in the body weight of the fasting individuals, compared to the non-fasting patients. By considering the role of weight gain or loss in NAFLD, the effect of altering weight on ALT in our fasting and non-fasting patients was not significant.

Various findings have been demonstrated in the studies focusing on the effect of Ramadan fasting on body weight. In some studies, a mild but statistically insignificant reduction in body weight has been reported during Ramadan within the range of 0.1-1.4 kg (14, 15). Some findings suggest that body weight and body fat percentage decrease significantly in fasting individuals from the beginning to the end of Ramadan by 1.9% and 6.2%, respectively and these indices increase significantly by 2.2% and 10.2% in the non-fasting individuals, respectively (16, 17). It seems that changes in the body weight during Ramadan is correlated with the cultural and social conditions of the populations studied in different countries.

Metabolic syndrome (obesity, systemic hypertension, dyslipidemia, insulin resistance, or overt diabetes) is an important cause of NAFLD and NASH. While some studies have reported increased total levels of cholesterol, HDL, and LDL in fasting individuals after Ramadan, other findings have reported increased high-density lipoprotein cholesterol and decreased blood cholesterol, triglyceride, low-density lipoprotein cholesterol, very-low-density lipoprotein cholesterol, and blood glucose (16-18). This discrepancy could be due to the differences in the eating habits, socioeconomic status, and rate of physical activity in Muslim communities.

In a study in this regard, mean morning concentration of leptin was observed to be significantly higher compared to the pre-Ramadan values, whereas adiponectin concen-

tration was significantly lower. These changes are associated with increased insulin resistance in the morning and evening during the month of Ramadan (19). Interestingly, in another study, the fasting subjects who experienced significantly decreased body weight also had a significant reduction in the plasma glucose, insulin level, and adiponectin, respectively. In addition, increased insulin sensitivity and diminished insulin resistance were among the other findings in these individuals (20). Changes in the body weight might play a pivotal role in obtaining heterogeneous results in this regard. With respect to cardiovascular risk factors, some studies have shown that Ramadan fasting is not associated with any changes in the incidence of acute cardiovascular disease and mean blood pressure (21-23).

A few studies have investigated the effect of fasting on liver function tests. In the rats with Ramadan-type fasting that were used as a model for Ramadan fasting in human, liver metabolic activities (e.g., liver lactate dehydrogenase, malate dehydrogenase, glucose-6-phosphatase, and fructose 1,6-bisphosphatase) were reported to enhance. Moreover, a significant increase was observed in the liver alkaline phosphatase, gamma-glutamyl transpeptidase, and leucine aminopeptidase (11). In another study focusing on chronic hepatitis, the fasting group had non-significant changes in the liver function tests prior to, during, and after the month of Ramadan. In the mentioned research, fasting cirrhotic patients developed significantly child class C cirrhosis during (13%) and after Ramadan (32.6%), compared to before Ramadan (0%) (24).

This was the first study to investigate the effect of Ramadan fasting on ALT in NAFLD. Patients with NAFLD had no significant reduction in body weight during Ramadan. If the body weight decreases significantly in Ramadan, the exact effects of Ramadan fasting on ALT in NAFLD patients are unknown, and to date, no studies have been conducted in this regard. Therefore, further investigations are required on larger samples sizes and various conditions, especially to determine the association of weight loss and education level in the NAFLD patients who fast in the holy month of Ramadan in order for a proper dietary regimen. Additionally, it is recommended that researchers evaluate the effects of Ramadan fasting on liver histology and fibrosis.

Conclusion

According to the results of the present study, Ramadan fasting may increase the level of ALT. In this regard, further investigations on larger sample sizes could focus on the patients with NAFLD who fast during Ramadan in order to verify the possible association between weight loss and education level to determine an effective dietary plan.

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