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Original Article

Effects of Ramadan Fasting on Muslim Patients with Liver Cirrhosis: A Comparative Study

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ABSTRACT

Background:
Patients with liver cirrhosis seem to be at increased risk of complications during fasting. This study aimed to assess the effect of Ramadan fasting on liver functions and portal hemodynamics among patients with liver cirrhosis in comparison with healthy subjects.

Materials and Methods:
Participants were divided into three groups. Group I: patients with liver cirrhosis who fasted during Ramadan (n = 34), group II: patients with cirrhosis who did not fast (n = 8), and group III: healthy volunteers who fasted (n = 30). This study was done from May 2017 to July 2017 and the month of Ramadan began on May 27th to June 26th, 2017. Portal hemodynamics were evaluated by portal vein diameter, congestion index (CI), and portal flow velocity. Laboratory investigations were determined before, during, and after Ramadan as an indicator of the changes in the liver functions.

Results:
There were no dropouts during the study. Among the three groups, portal vein parameters showed statistically non-significant differences. Model for End stage Liver Disease (MELD) score and serum albumin levels showed a significant difference when the group I and II compared separately to group III ($p = 0.000$), while there were no differences between group I and group II ($p = 0.6$ and 0.57, respectively). For portal vein CI, there was a significant difference between the patients with cirrhosis (fasting; group I and non-fasting; group II) and healthy subjects (group III) ($p = 0.000$), while the CI did not change significantly between the groups I and II ($p = 0.54$).

Conclusion:
Patients with cirrhosis showed changes in their liver functions and portal hemodynamics irrespective of their fasting status and these differences were more pronounced in portal vein CI, MELD score, and serum albumin when compared with healthy subjects.

Keywords: Cirrhosis, Ramadan fasting, MELD score, Portal vein, Congestion index

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INTRODUCTION

Ramadan, the holy month for Muslims, is a lunar-based month, which rotates around the year. During the month eating, drinking, smoking, or using oral medications are prohibited from predawn to sunset. Due to the rotation around the year, this month occurred in the summertime in the Northern hemisphere over the last few years, with a very long period of daytime fasting (1-3).

In the literature, the data focusing on the impact of

fasting on liver function are scarce. Relying on the current evidence, patients with liver cirrhosis seem to be at increased risk of complications during fasting. Expected complications include protein-energy malnutrition, upper gastrointestinal bleeding (UGIB), deterioration of liver functions, and development of hepatic encephalopathy (HE) (4-6). In an earlier study, we followed up a group of fasting patients with liver cirrhosis during the summertime, and reported the deleterious impact of fasting on patients with Child-class B and C. Deteriorations noticed were advanced Child classes, development of lower limb edema, increasing ascites, increasing jaundice, and development of overt encephalopathy (2).

Consequently, patients with cirrhosis should be thoroughly evaluated before being allowed to fast and care must be tailored to every patient and even for the same patient from one year to another (4). According to the current evidence patients with Child class C should not fast, and patients with Child B need careful assessment for manifestations of liver deterioration before they fast (3,6).

This study aimed to assess the whole month of Ramadan fasting during the summer time on liver functions and portal hemodynamics among patients with liver cirrhosis in comparison with healthy subjects.

MATERIALS AND METHODS

This study was done in the Internal and Tropical Medicine Departments, Zagazig University Hospitals, Sharkia Governorate, Egypt from May 2017 to July 2017 and the month of Ramadan began on May 27th to June 26th, 2017. Patients were recruited from both the outpatient clinics as well as inpatient wards. Portal hemodynamics were evaluated by portal vein diameter, congestion index (CI), and portal flow velocity. Laboratory investigations were determined before, during, and after Ramadan as an indicator of the changes in the liver functions.

Inclusion criteria

- Patients with liver cirrhosis Child class A
- Patients with liver cirrhosis Child class B have discussed the risk of fasting and offered not to fast
- Assumed availability during the study
- Willing to participate

Exclusion criteria

Patients with Child class C, patients with confirmed hepatocellular carcinoma (HCC), and patients with overt hepatic encephalopathy (HE). Patients with any renal impairment, chronic obstructive pulmonary disease (COPD), diabetes, and heart failure were also excluded from the study.

All patients were subjected to:

1. Full history taking.
2. Thorough physical examination.
3. Laboratory investigations, including complete blood count, kidney function tests, liver function tests (serum albumin, bilirubin, alanine transferase (ALT), aspartate transferase (AST), prothrombin time, and concentration), viral markers (HBsAg, hepatitis c virus antibodies) and alfa-fetoprotein (AFP). Abdominal ultrasonography for the assessment of liver size, echogenicity, focal lesions, and presence of ascites and splenomegaly and determination of portal vein patency.
4. Doppler ultrasonography on the portal vein using real-time ultrasonography with 3.5 MHz transducers and a pulsed Doppler device (Medison, 8000 EX, Korea) to determine portal vein (PV) diameter, flow velocity, and CI (7).
5. Medications that were given after Iftar and Sohor. Diuretics were taken after Iftar (early night) to minimize daytime exhaustion.
6. Dietary advice. Sohor (is the last diet before dawn) was postponed until the time of dawn and Iftar (first food after sunset) was taken just with the evening and the patients were asked to take plenty of fluids in between, with a midnight snack. They were advised to avoid direct exposure to the sunlight and stay at home during the daytime.
7. Instructions for emergency admission in the hospital if they developed any complications including bleeding, encephalopathy, fever, increasing ascites, or any major health problem.

Ethical approval

All the participants provided written informed consent to participate in the study and to perform all relevant interventions.

Table 1: Demographics of all groups

Variables	Group I (N = 34)	Group II (N = 8)	Group III (N = 30)	*P* value
Age (years) (Mean ± SD)	54 ± 8.8	54.5 ± 11.7	53.3 ± 13.1	0.71
Gender (number) Male/Female	16/18	4/4	15/15	0.90

Table 2: Portal vein parameters

Variables	Group I (n = 34)		Group II (n = 8)		Group III (n = 30)		*P* value
	Before	After	Before	After	Before	After	
Portal Vein Diameter (Mean ± SD)	14.05 ± 1.63	14.20 ± 1.53	14.25 ± 2.25	14.50 ± 1.77	11.36 ± 1.71	11.63 ± 1.51	0.94
Portal Vein Congestive Index (Mean ± SD)	0.132 ± 0.049	0.125 ± 0.046	0.145 ± 0.029	0.140 ± 0.071	0.069 ± 0.033	0.091 ± 0.118	0.53
(Portal Vein flow Velocity (Mean ± SD)	12.06 ± 3.21	13.21 ± 3.54	10.88 ± 2.232	12.62 ± 3.37	15.27 ± 5.49	15.80 ± 4.92	0.65

Statistical analysis

Data were checked, entered, and analyzed using SPSS software, version 15 (SPSS Inc., Chicago, Illinois, USA). Data were expressed as number and percentage (analyzed by Wilcoxon test for paired qualitative variables) and as mean ± SD (analyzed by a paired t test for quantitative variables). A P value less than 0.05 was considered as statistically significant.

RESULT

Basal characteristics

The participants (table 1) were divided into three groups. The group I included patients with liver cirrhosis who fasted during Ramadan (n = 34), group II included patients with cirrhosis who were advised not to fast during Ramadan (n = 8), while group III included healthy fasting volunteers (n = 30). The baseline characteristics of the studied groups are shown in table 1 with no significant differences in demographics. There were no dropouts, and all the patients were followed up until the end of the study.

Portal vein hemodynamics

Portal vein variables are shown in table 2. Among the three groups, portal vein parameters (diameter, velocity, and CI) showed statistically non-significant differences (*p* values 0.94, 0.53, and 0.65 respectively). In all groups, portal vein blood velocity increased after fasting compared with before fasting, although the difference among the three groups was not statistically significant. The portal vein diameter showed minor changes in all groups following the fasting state. There was a reduction of portal vein CI in patients with cirrhosis (fasting and non-fasting) while it was increased in healthy subjects after fasting.

Liver functions

The laboratory parameters of each group are shown in the tables 3-5. For fasting patients with cirrhosis (group I) there was evidence of deteriorations in some benchmarks, but with no statistical significance. Serum bilirubin is an excellent example of biochemical declines induced by fasting. It increased from 1.17 ± 1.07 mg/dL before fasting to 2.17 ± 1.98 mg/dL after one month of continuous fasting. The same also applied for the international normalized ratio (INR) and serum creatinine, and that is why MELD score increased from 8.47 ± 8.156 before fasting to 14.31 ± 9.76 after fasting. Liver enzymes showed minor elevations while serum albumin and platelet counts showed minor decreases (table 3).

For non-fasting patients with liver cirrhosis (group II), there was evidence of deteriorations in some parameters, consistent with the natural history of cirrhosis including serum bilirubin, INR, serum albumin, creatinine, platelets, and MELD score, although these did not reach the degree of statistical significance. Liver enzymes showed minor elevations of AST and small drops in ALT (table 4).

In fasting healthy subjects (group III), mild changes in the biochemical markers occured and were evident in liver enzymes, which increased by the end of the Ramadan. Minor non-significant changes in hemoglobin, bilirubin, and INR were also reported (table 5).

Table 3: Laboratory parameters of group I patients during the study period

Variables	Before Ramadan (one month)	During Ramadan	After Ramadan (one month)	*P* value
Hemoglobin (gm/dl)	11.61 ± 1.52	11.78 ± 1.40	12.07 ± 1.79	0.40
Bilirubin (mg/dl)	1.17 ± 1.07	1.204 ± 1.2	1.27 ± 1.98	0.36
Creatinine (mg/dl)	0.92 ± 0.21	0.90 ± 0.26	0.97 ± 0.11	0.52
INR	1.03 ± 0.1	1.12 ± 0.3	1.28 ± 0.43	0.65
MELD	13.47 ± 8.156	13.56 ± 6.11	14.31 ± 9.760	0.64
Albumin (gm/dl)	3.73 ± 0.52	3.60 ± 0.61	3.54 ± 0.80	0.51
Platelets (x103)	139.85 ± 77.93	137.34 ± 52.12	136.21 ± 68.40	0.53
AST (IU/L)	35.65 ± 17.82	35.90 ± 15.70	43.40 ± 16.30	0.43
ALT (IU/L)	35.34 ± 27.92	38.57 ± 28.25	44.18 ± 24.44	0.51

Table 4: Laboratory parameters of group II patients during the study period

Variables	Before Ramadan	During Ramadan	After Ramadan	*P* value
Hemoglobin (gm/dl)	11.14 ± 2.60	11.42 ± 2.76	9.42 ± 1.511	0.43
Bilirubin (mg/dl)	0.85 ± 0.37	1.02 ± 0.37	1.14 ± 0.69	0.42
Creatinine (mg/dl)	0.74 ± 0.377	0.85 ± 0.37	1.0 ± 0.00	0.53
INR	1.25 ± 1.00	1.27 ± 0.60	1.28 ± 0.48	0.66
MELD	14.57 ± 2.69	14.61 ± 4.79	14.85 ± 2.13	0.60
Albumin (gm/dl)	3.23 ± 0.57	3.24 ± 0.70	3.28 ± 0.95	0.53
Platelets (x103)	139.85 ± 77.93	129.85 ± 79.96	86.00 ± 2.29	0.54
AST (IU/L)	48.57 ± 24.26	32.00 ± 11.74	54.60 ± 73.39	0.52
ALT (IU/L)	38.57 ± 28.25	25.14 ± 9.63	17.00 ± 2.64	0.53

Table 5: Laboratory parameters of group III patients during the study period

Variables	Before Ramadan	During Ramadan	After Ramadan	*P* value
Hemoglobin (gm/dl)	12.76 ± 1.38	13.76 ± 1.68	12.25 ± 1.16	0.45
Bilirubin (mg/dl)	1.04 ± 0.36	1.07 ± 0.40	1.10 ± 0.43	0.40
Creatinine (mg/dl)	0.99 ± 0.23	0.96 ± 0.14	0.96 ± 0.14	0.56
INR	6.19 ± 19.79	0.99 ± 0.03	0.99 ± 0.03	0.64
MELD	9.31 ± 2.48	9.47 ± 3.21	9.53 ± 2.95	0.61
Albumin (gm/dl)	4.27 ± 0.46	4.03 ± 0.33	4.03 ± 0.21	0.46
Platelets (x103)	239.13 ± 68.67	214.23 ± 70.89	220.03 ± 56.66	0.43
AST (IU/L)	28.63 ± 13.87	41.13 ± 48.09	54.60 ± 73.39	0.45
ALT (IU/L)	26.23 ± 12.77	40.00 ± 44.47	51.00 ± 67.68	0.44

Between the groups

When the three groups were compared regarding the biochemical parameters at the baseline and after ending the one month of fasting, there were significant differences among the three groups regarding MELD score and serum albumin levels. When MELD score and serum albumin levels were compared between fasting patients with cirrhosis (group I) and healthy subjects and between non-fasting patients with cirrhosis (group II) and healthy subjects the *P* values = 0.000 for all comparisons, while there were no differences between fasting patients with cirrhosis (group I) and non-fasting patients with cirrhosis (group II) for MELD score and serum albumin (p = 0.6 and 0.57, respectively). For portal vein CI the same was also reported. There was a significant difference between patients with cirrhosis (fasting; group I and non-fasting; group II) and healthy subjects (group III) (p = 0.000), while the portal vein CI did not change significantly between group I and II (p = 0.54).

DISCUSSION

In the last few years, several studies focusing on the impact of fasting on liver functions had been published. One of these studies was done by our research team in 2014 (2), and we reported at that time deteriorations in liver functions and portal hemodynamics besides clinical decompensation. However, one major limitation of that study was the lack of a comparative group, and that was recognized in the current study. Another primary concern was the use of Child classification for the assessment of hepatic deterioration. Because it had some subjective variables, e.g., ascites, and Hepatic Encephalopathy (HE), we used MELD evaluation score in the current study.

We compared a cohort of patients with liver cirrhosis who intended to complete the holy month fasting with another group of patients with liver cirrhosis who were advised not to fast and also a group of apparently healthy fasting subjects who completed the whole month fasting.

Previous studies (8-10) reported minor, mostly non-significant changes in liver biochemistry including AST, ALT, ALP, and bilirubin among healthy subjects. Furthermore, significant changes were also reported among patients with liver cirrhosis (2,5) who completed one month of Ramadan fasting.

In the current study, these changes were also reported. For patients with liver cirrhosis, it seems that changes happened in both fasting and non-fasting groups, but were more pronounced in the fasting group. This confirms that the natural history of cirrhosis is an additive factor for deteriorations reported among patients with liver cirrhosis that cannot solely be explained by fasting. The changes were more evident in the levels of serum bilirubin, albumin, and liver enzymes.

For healthy subjects in our study, there were minor rises of AST, ALT, and bilirubin and small drops of hemoglobin and albumin, all of which were non-significant. Consequently, healthy adults can withstand the whole month of fasting without any expected deterioration because these biochemical changes are clinically insignificant (10,11).

For portal vein hemodynamics, all the parameters showed non-significant changes among the three groups. However, when the CI index was compared separately between healthy subjects and each cirrhotic group it was evident that CI increased in patients with liver cirrhosis, which is a similar finding that we reported in our previous study (2). However, the confusion is that both fasting and non-fasting patients with cirrhosis showed the same significant change in CI in comparison with healthy subjects. This was not possible to conclude in our previous study (2) due to the lack of a comparative group and again this may accuse the natural history of cirrhosis as a main prognostic factor in this issue and not only the fasting.

MELD score and serum albumin are reflective of liver functions, and when cirrhotic fasting and non-fasting groups were compared with healthy subjects, there was evidence of liver function deterioration in patients with liver cirrhosis. Whereas, the difference between cirrhotic fasting and non-fasting groups was not significant and this again was consistent with progression of cirrhosis.

This study corrected some limitations in our previous study (2) notably including groups of both healthy individuals and patients with liver cirrhosis and exclusion of patients with Child class C. However, still, the current study has some limitations, including the small number of patients in the cirrhotic non-fasting group, being a single center study, and lack of long-term follow-up to monitor morbidity and mortality over time.

In conclusion, patients with cirrhosis over the holy month Ramadan in 2017 showed changes in their liver functions and portal hemodynamics irrespective of their fasting status and these differences were more pronounced in portal vein CI, MELD score, and serum albumin when compared with healthy subjects. Consequently, hepatic function reserve seems to be the most critical factor and should be assessed in every patient by different means.

CONFLICT OF INTEREST

The authors declare no conflict of interests related to this work.

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