Evaluation of Thyroid Functions in Cirrhotic Patients with Refractory Ascites

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Background and study aim: Disturbance of thyroid functions was observed in patients with advanced liver cirrhosis. This study aimed to assess thyroid hormone levels in cirrhotic patients and to evaluate the relationship between thyroid function disturbances and cirrhotic patients with refractory ascites.

Methods: This study included 244 cirrhotic patients enrolled into 3 groups: group A included 122 cirrhotic patients with refractory ascites, group B included 62 cirrhotic patients with ascites and Group C included 60 cirrhotic patients without ascites. All patients were evaluated by complete blood count, liver functions, kidney functions, coagulation profiles, serology for viral hepatitis, serum Na, serum K, urine analysis, thyroid function tests, and abdominal ultrasonography.

Results: In group A, 21.3 % of patients had high TSH levels, 14.8 % had low free T3 levels and 9.8 % had low free T4 levels. Cirrhotic patients with refractory ascites had a statically significant lower levels of free T3 (2.43 ± 0.66) and free T4 (1.16 ± 0.21) (P > 0.05), but no significant difference as regard TSH levels compared to cirrhotic patients without ascites. Child C cirrhotic patients had a statistically significantly lower levels of free T3 (2.44 ± 0.68) and free T4 (1.16 ± 0.21) compared to child A cirrhotic patients (P > 0.05).

Conclusion: The percentage of elevated TSH levels and decreased free T3 and T4 levels was more in cirrhotic patients with refractory ascites. Hypothyroidism could be a risk factor for the occurrence of refractory ascites in patients with advanced liver cirrhosis .

INTRODUCTION

Ascites is one of the most common complications of cirrhosis. More than 50 % of cirrhotic patients will develop ascites within 10 years **[1].** In cirrhotic patients, the survival rate is only 50% at two to five years from the onset of ascites and 5 % to 10 % of ascitic patients per year become resistant to standard diuretics which is called refractory ascites **[2].** According to the International Ascites Club criteria, refractory ascites is ascites that can't respond or recurs early after therapeutic paracentesis and can't be satisfactorily prevented by medical therapy such as high-dose diuretics and sodium restriction. Refractory ascites is classified into two subtypes: diuretic-resistant ascites and diuretics intractable ascites **[3].**

One of the possible risk factors that may lead to refractory ascites is a disturbance of thyroid functions. The liver plays an important role in the metabolism of thyroid hormones, as it is the most important organ in the peripheral conversion of tetraiodothyronine (T4) to triiodothyronine (T3) by Type 1 deiodinase. Moreover, the liver is involved in thyroid hormone conjugation and excretion, as well as the synthesis of thyroid-binding globulin. T4 and T3 regulate the basal metabolic rate of all cells, including hepatocytes, and thereby modulate hepatic function. The liver metabolizes the thyroid-stimulating hormone (TSH) and regulates its systemic endocrine effects **[4][5].** Results of available studies in different populations are variable, but

the most frequent changes were decreased total T3 and free T3 levels which are reported to be associated with the severity of liver impairment. More studies on thyroid functions in patients with liver cirrhosis and ascites are needed to gain a better knowledge of the interrelationship between thyroid functions and liver cirrhosis, which could aid in the management of cirrhotic patients, particularly those with refractory ascites. This study aimed to assess thyroid hormone levels (TSH, free T3, and free T4) in patients with liver cirrhosis and evaluate the relationship between thyroid functions and cirrhotic patients with refractory ascites.

PATIENTS AND METHODS

This study included 244 cirrhotic patients recruited from the outpatient clinics and emergency units of the Tropical Medicine Department, Zagazig University Hospitals and Hepatic Department, Zagazig Fever Hospital, in the period between September 2020 to August 2021.

Inclusion criteria:

All included 244 patients were cirrhotic (cirrhosis diagnosis based on clinical, biochemical, and imaging studies), then patients enrolled into 3 groups:

- Group A included cirrhotic patients with refractory ascites (122 patients) according to the International Ascites Club criteria **[3].**
- Group B included cirrhotic patients with ascites (62 patients) who have ascites according to the clinical and ultrasound findings and don't follow International Ascites Club criteria for refractory ascites **[3].**
- Group C included cirrhotic patients without ascites (60 patients) who have liver cirrhosis with an absence of ascites clinically and in abdominal ultrasound examination.

Exclusion criteria:

- Known cases of thyroid disorder without liver cirrhosis.
- Patients previously treated with interferon.
- Patient with a history of organ failure, cancer, radio, or chemotherapy.

Patient assessment: All patients were subjected to the following:

- Thorough history taking (regarding symptoms of liver cirrhosis and thyroid diseases).
- Complete physical examination (including clinical signs of liver cirrhosis, clinical signs of thyroid diseases, and grade of ascites if present).
- Child-Pugh scoring.
- Laboratory studies included complete blood count, liver functions, kidney functions, coagulation profiles, serology for viral hepatitis, serum Na, serum K, urine analysis and thyroid function tests (TSH, free T3, and free T4). Ascitic fluid samples analysis from patients with ascites for estimation of ascitic fluid protein, white blood cell count, and serum ascites albumin gradient (SAAG).
- Abdominal ultrasonography: The participants were examined by Mindray diagnostic ultrasound system (DC-N2) at Zagazig University Hospital and GE logic p3 at Zagazig Fever Hospital while fasting for 6 hours at least. The liver size, surface, echogenicity, hepatic veins, and portal vein were commented upon. Hepatic focal lesions' number, location, and size are all determined, and if present patients were excluded from the study. Also, the size, the texture of the spleen, and the presence of ascites were assessed. Ascites was classified according to its amount into mild (free fluid in the pelvis and the hepatorenal pouch), moderate (free fluid in the flanks), and massive (free fluid in the central part of the abdomen and around the intestine).

Statistical analysis

The collected data were computerized and statistically analyzed using the SPSS program (Statistical Package for Social Science) version 24 and NCSS 12, LLC, USA. Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi-square test ($\chi 2$) and Fisher exact were used to calculate the difference between qualitative variables as indicated. Quantitative data were expressed as median and range. Mann-Whitney test was used to calculate the difference between quantitative variables in two groups for non-normally distributed variables. Kruskal-Wallis Test was used to calculate the difference between quantitative variables in more than two groups for non-normally distributed variables. Post hoc test for multiple comparisons was done by using Dunn's Multiple Comparison Post-hoc test, to indicate which groups were significantly different from each other. All statistical

comparisons were two-tailed with a significance Level of P-value ≤ 0.05 indicates significant difference, p < 0.001 indicates a highly significant difference while P > 0.05 indicates a non-significant difference.

RESULTS

This study included 244 cirrhotic patients which were divided into 3 groups according to presence and degree of ascites; group A: 122 cirrhotic patients with refractory ascites, group B: 62 cirrhotic patients with ascites, and group C: 60 cirrhotic patients without ascites. The mean age of all studied patients was 60.32 ± 6.43 years old with a median of 60 years old, and a range of (44 – 81 years old). Most of the included patients (51.2%) were female. 91.8 % of studied patients were positive for chronic hepatitis C virus (HCV), 3.3 % were positive for chronic hepatitis B virus (HBV) and 4.9 % were negative for both HCV and HBV. There was no statistically significant difference between the studied groups as regard age, sex, and cause of cirrhosis (Table 1). Cirrhotic patients with refractory ascites presented with jaundice (80.3%), splenomegaly (83.6%), lower limb edema (100 %), and 73.8 % of them had hepatic encephalopathy. Cirrhotic patients with ascites presented with jaundice (25.8%), splenomegaly (83.9%), lower limb edema (67.7 %), and only 8 patients had hepatic encephalopathy. In cirrhotic patients without ascites, 3.3 % of patients had jaundice, 26.7 % had splenomegaly and 15 % had lower limb edema. According to Child-Pugh classification, all cirrhotic patients with refractory ascites were child class C with a mean score of 11.9 ± 1.05; cirrhotic patients with ascites were child class B (87.1 %) and child class C (12.9 %), and 96.7 % of cirrhotic patients without ascites were child class A. Table 2; shows the distribution of thyroid function among the studied groups. In group A, 21.3 % of patients had high TSH levels, 14.8 % had low free T3 levels and 9.8 % had low free T4 levels. In group B, 19.4 % of patients had high TSH levels, 14.5 % had low free T3 levels and 9.7 % had low free T4 levels. In group C, 11.7 % of patients had high TSH levels, 11.7 % had low free T3 levels and 6.7 % had low free T4 levels. In comparison between 3 groups, there was a statistically significant difference as regard free T3 levels and free T4 levels mainly between cirrhotic with refractory ascites (2.43 ± 0.66 & 1.16 ± 0.21, respectively) and cirrhotic without ascites (2.7 ± 2.65 & 1.25 ± 0.20, respectively) (P < 0.05) (Fig. 1), but no significant difference as regard TSH (Fig. 2) (Table 3). According to the Child-Pugh classification of all included patients, high TSH level was observed in 22.7 % of child C patients, 14.8 % of child B patients, and 7 % of child A patients. Low free T3 level was observed in 15.9 % of child C patients and 12.1 % of child A patients. Low free T4 level was observed in 9.8% of child C patients and 6.9% of child A patients (Table 4). There was a statically significant difference between child A patients and child C patients as regard serum levels of free T3 and free T4 with low free T3 level (2.44 ± 0.68) and free T4 level (1.16 ± 0.21) in child C patients (P < 0.05) (Table 5) (Fig. 3). All patients in group A received spironolactone & furosemide as intensive diuretic drugs. There was a lack of response to diuretics in 48.4 % of these patients. All refractory ascites patients showed early recurrence of ascites. 73.8% of patients in group A complained of diuretic-induced hepatic encephalopathy and 21.3 % of them had diuretic-induced renal impairment. About 69.7% of refractory ascites patients had diuretic-induced hyponatremia and 68% had diuretic-induced hypokalemia or hyperkalemia. We assessed the relation between thyroid dysfunction, and factors associated with the development of refractory ascites in group A. There was a significant relation between high TSH level with lack of response to diuretics, diuretic-induced renal impairment, diuretic-induced hypokalemia or hyperkaliemia and hepatic encephalopathy (P<0.05) (Table 6).

Table (1): Demographic characteristics and cause of cirrhosis in the studied groups.

Variables		Group A N=122	Group B N=62	Group C N=60	Total N=244	P
Age (years) Mean ± SD		60.34 ± 7.15	60.37 ± 5.36	60.23 ± 5.99	60.32 ± 6.43	0.968* (NS)
		N (%)	N (%)	N (%)	N (%)	
Gender	Female	62 (50.8%)	32 (51.6%)	31 (51.7%)	125 (51.2%)	0.992† (NS)
	Male	60 (49.2%)	30 (48.4%)	29 (48.3%)	119 (48.8%)	
Cause of cirrhosis	HCV	112 (91.8%)	57 (92.0%)	55 (91.7%)	224 (91.8%)	0.999† (NS)
	HBV	4 (3.3%)	2 (3.2%)	2 (3.3%)	8 (3.3%)	
	Non-HCV Non-HBV	6 (4.9%)	3 (4.8%)	3 (5.0%)	12 (4.9%)	

NS= non-Significant
*Mann-Whitney test
†Chi square test

Table (2): Distribution of thyroid function among the study groups.

		Group A N=122	Group B N=62	Group C N=60	Total N=244	P
		N (%)	N (%)	N (%)	N (%)	
TSH Level	Normal	90 (73.8%)	48 (77.4%)	52 (86.7%)	190 (77.9%)	0.389* (NS)
	High	26 (21.3%)	12 (19.4%)	7 (11.7%)	45 (18.4%)	
	Low	6 (4.9%)	2 (3.2%)	1 (1.7%)	9 (3.7%)	
Free T3 Level	Normal	104 (85.2%)	53 (85.5%)	53 (88.3%)	210 (86.1%)	0.842* (NS)
	Low	18 (14.8%)	9 (14.5%)	7 (11.7%)	34 (13.9%)	
Free T4 Level	Normal	110 (90.2%)	56 (90.3%)	56 (93.3%)	222 (91.0%)	0.765* (NS)
	Low	12 (9.8%)	6 (9.7%)	4 (6.7%)	22 (9.0%)	

NS= non-Significant.
* Chi square test

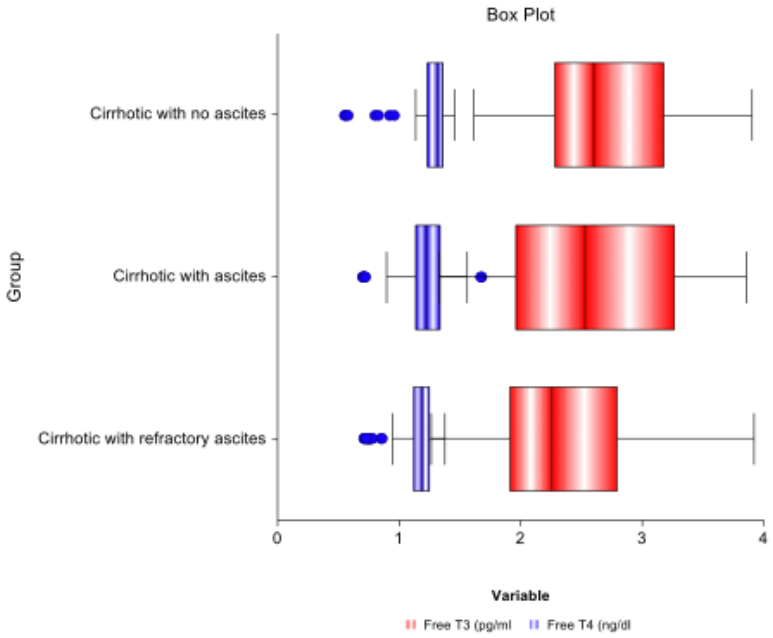

Fig. (1): Box-plot diagram represents the range of Free T3 (pg/ml) and Free T4 (ng/dl) in the studied groups.

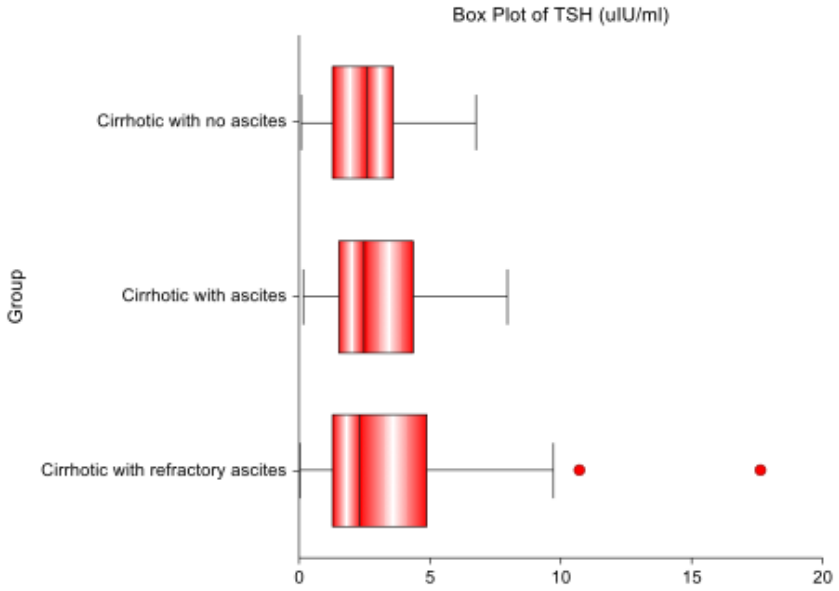

Fig. (2): Box-plot diagram represents the range of TSH (uIU/ml) in the studied groups.

Table (3): Comparison between 3 groups as regard serum level of TSH, free T3 and free T4.

	Group A N=122	Group B N=62	Group C N=60	Total N=244	Each 2 groups	P
TSH (uIU/ml) Mean ± SD Median (Range)	 3.23 ± 2.8 2.33 (0.05-17.6)	 3.14 ± 2.19 2.46 (0.17-7.9)	 2.85 ± 1.94 2.6 (0.06-6.7)	 3.12 ± 2.46 2.4 (0.05-17.6)		0.826* (NS)
Free T3 (pg/ml) Mean ± SD Median (Range)	 2.43 ± 0.66 2.26 (1.26-3.92)	 2.59 ± 0.75 2.5 (1.3-3.86)	 2.7 ± 2.65 2.6 (1.62-3.9)	 2.54 ± 0.69 2.39 (1.26-3.9)	P1=0.13 P2=0.01 P3=0.336	0.013* (S)
Free T4 (ng/dl) Mean ± SD Median (Range)	 1.16 ± 0.21 1.18 (0.71-2.16)	 1.21 ± 0.22 1.2 (0.70-1.68)	 1.25 ± 0.20 1.3 (0.5-1.46)	 1.19 ± 0.21 1.2 (0.55-2.16)	P1=0.114 P2=0.008 P3=0.337	<0.001* (HS)

NS= non-Significant.
S= Significant.
HS= High-Significant.
* Kruskal Wallis test.
P1=group A Vs group B, P2= group A Vs group C, P3= group B Vs group C.

Table (4): Distribution of thyroid functions in studied patients according to Child Pugh Classification.

		Child Pugh classification			P
		A	**B**	**C**	
		N (%)	N (%)	N (%)	
TSH Level	Normal	50 (86.2%)	44 (81.5%)	96 (72.7%)	0.297* (NS)
	High	7 (12.1%)	8 (14.8%)	30 (22.7%)	
	Low	1 (1.7%)	2 (3.7%)	6 (4.5%)	
Free T3 Level	Normal	51 (87.9%)	48 (88.9%)	111 (84.1%)	0.620* (NS)
	Low	7 (12.1%)	6 (11.1%)	21 (15.9%)	
Free T4 Level	Normal	54 (93.1%)	49 (90.7%)	119 (90.2%)	0.805* (NS)
	Low	4 (6.9%)	5 (9.3%)	13 (9.8%)	

NS= non-Significant.
* Chi square test.

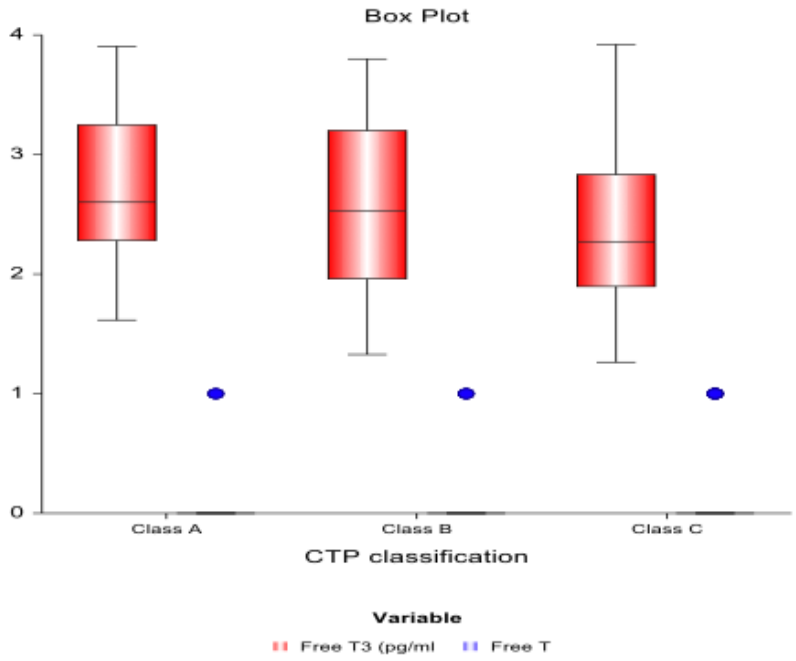

Fig. (3): Box-plot diagram represents the range of Free T3 (pg/ml) and Free T4 (ng/dl) in the studied patients after classification into 3 groups according to Child-Pugh scoring.

Table (5): Comparison between serum level of TSH, free T3 and free T4 as regard Child Pugh Classification.

	Child Pugh classification			Each 2 groups	P
	A	**B**	**C**		
TSH (uIU/ml) Mean ± SD Median (Range)	 2.91± 1.95 2.66 (0.06-6.75)	 2.85 ± 2.04 2.38 (0.17-7.95)	 3.32 ± 2.79 2.36 (0.05-17.63)		0.381* (NS)
Free T3 (pg/ml) Mean ± SD Median (Range)	 2.71 ± 0.65 2.60 (1.62-3.90)	 2.59 ± 0.71 2.53 (1.33-3.80)	 2.44 ± 0.68 2.28 (1.26-3.92)	P1=0.366 P2=0.012 P3=0.157	0.033* (S)
Free T4 (ng/dl) Mean ± SD Median (Range)	 1.24 ± 0.21 1.32 (0.55-1.46)	 1.22 ± 0.22 1.25 (0.70-1.67)	 1.16 ± 0.21 1.18 (0.71-2.16)	P1=0.465 P2=0.014 P3=0.119	0.033* (S)

NS= non-Significant.
S= Significant.
* Kruskal Wallis test.
P1=group A Vs group B, P2= group A Vs group C, P3= group B Vs group C.

Table (6): Relation between TSH level and studied parameters among the refractory ascites group (group A).

		TSH Level			P
		Normal N=90	High N=26	Low N=6	
		N (%)	N (%)	N (%)	
Cause of cirrhosis	HCV	73 (81.1%)	24 (92.3%)	5 (83.3%)	0.632* (NS)
	HBV	7 (7.8%)	1(3.8%)	0 (0.0%)	
	Non-HCV Non-HBV	10 (11.1%)	1 (3.8%)	1 (16.7%)	
Lack of response	Absent	51(56.7%)	8 (30.8%)	4 (66.7%)	0.05* (S)
	Present	39 (43.3%)	18 (69.2%)	2 (33.3%)	
Diuretic-induced hepatic encephalopathy	Absent	28 (31.1%)	2 (7.7%)	2 (33.3%)	0.053* (S)
	Present	62 (68.9%)	24 (92.3%)	4 (66.7%)	
Diuretic-induced renal impairment	Absent	76 (84.4%)	18 (69.2%)	2 (33.3%)	0.005* (S)
	Present	14 (15.6%)	8 (30.8%)	4 (66.7%)	
Diuretic-induced hyponatremia	Absent	29 (32.2%)	8 (30.8%)	0 (0.0%)	0.251* (NS)
	Present	61 (67.8%)	18 (69.2%)	6 (100.0%)	
Diuretic-induced hypokalemia or hyperkaliemia	Absent	25 (27.8%)	14 (53.8%)	0 (0.0%)	0.01* (S)
	Present	65 (72.2%)	12 (46.2%)	6 (100.0%)	
Jaundice	Absent	74 (82.2%)	20 (76.9%)	4 (66.7%)	0.576* (NS)
	Present	16 (17.8%)	6 (23.1%)	2 (33.3%)	
Hepatomegaly	Absent	80 (88.9%)	20 (76.9%)	4 (66.7%)	0.133* (NS)
	Present	10 (11.1%)	6 (23.1%)	2 (33.3%)	
Splenomegaly	Absent	18 (20.0%)	2 (7.7%)	0 (0.0%)	0.177* (NS)
	Present	72 (80.0%)	24 (92.3%)	6 (100.0%)	

NS= non-Significant.
S= Significant.
* Chi square test.

DISCUSSION

Approximately 60% of patients with cirrhosis will develop ascites within 10 years after diagnosis of this disease. Refractory ascites will develop in 5 % - 10 % of cirrhotic patients with ascites **[6].** Patients with refractory ascites carry a 1-year mortality rate about 70%, and more than 50% of these patients will develop hepatorenal syndrome **[7].** Cirrhotic patients with ascites should be monitored closely, and possible factors leading to refractory ascites should be identified and treated. One of the possible risk factors that may lead to refractory ascites is disturbance of thyroid functions. This study aimed to assess thyroid hormones levels (free T3, free T4, and TSH) in patients with liver cirrhosis and evaluating the relationship between the thyroid functions and cirrhotic patients with refractory ascites.

In the present study, all included patients were cirrhotic and the cause of cirrhosis was chronic HCV infection (91.8%), chronic HBV infection (3.3 %), and non-viral etiology (4.9 %), respectively. The main etiology for cirrhosis in our study is chronic HCV infection. Egypt was known for its high prevalence rate of HCV infection in the world as reported by the WHO in 2016 and based on the data from the Egyptian Health Issue Survey in 2015, it was estimated that approximately 3.7 million persons in Egypt suffer from HCV infection **[8].** In contrast, previous studies evaluated thyroid function in cirrhotic patients, alcoholism was the most common cause of cirrhosis in these studies followed by chronic HCV and HBV infection **[9][10].** The mean age of the included patients was 60.32 ± 6.43 years, and this reflects those patients were infected during their active phases of life being subjected to the different risk factors of HCV infection and then developed cirrhosis. There was no statistically significant difference between the studied groups as regard age, sex, and cause of cirrhosis.

Regarding the distribution of thyroid function among patients in this study (Table 2), the most seen abnormalities were high TSH level in 18.4

% of patients and low free T3 level in 13.9 % of patients, and low free T4 level in 9 % of patients. All these cirrhotic patients did not have any clinical signs of hypothyroidism and their TSH levels were also in the subclinical range of hypothyroidism. Inconsistent with our results, Punekar et al., 2018, reported high TSH levels in 20% of cirrhotic decompensated patients and low free T3 levels in 41% of these patients. Also, all patients did not have any clinical signs of hypothyroidism **[11].** In contrast, in a study by Samarthana & Mamatha, 2020, 64 cases (64 %) out of 100 patients had high TSH levels and 63 (63%) patients had serum T3 levels less than 0.4 pg/ml **[10].** The high prevalence of hypothyroidism in this study compared to our study could be due to the etiology of liver cirrhosis in this study which was alcoholism in 85% of patients. Alcoholism may be a co-factor for the increased prevalence of hypothyroidism as alcohol intake has been associated directly with impaired hepatic deiodinase activity **[12].** However, Mobin et al., 2016 reported that in all decompensated cirrhotic patients (sample size n = 76), 76.3% had low serum T3 levels, 14.47% had low serum T4 levels, and only 2.63% had raised TSH levels (18.4 % in our study) **[13].** This difference between studies could be due to sample size, the severity of liver disease, regional variation of thyroid disorders, and cause of liver cirrhosis (chronic HCV in Egypt and alcoholism in western countries).

In comparison between 3 groups in our study, there was a statistically significant difference as regard free T3 level and free T4 level mainly between cirrhotic with refractory ascites (group A) and cirrhotic without ascites (group C) ($P < 0.05$), but no significant difference as regard TSH level between the three groups. Patients in group A have advanced liver cirrhosis with refractory ascites which may have marked abnormalities in serum concentrations of thyroid hormone-binding proteins. Also, advanced cirrhosis cause inhibition of type 1 deiodinase activity, which causes the decreased conversion of T4 to T3, as well as preserved activity of type 2 deiodinase, causing increased T4 conversion into reverse T3 **[11].** Furthermore, poor nutrition and cytokines such as Interleukin-6 may explain decreased free T3 levels in patients with advanced liver cirrhosis **[14].** This finding is consistent with Punekar et al., 2018 and Kayacetin et al. 2003 who reported that serum levels of free T3 and total T4 were significantly lower in all cirrhotic patients **[11][15].** Similarly, several studies reported that the levels of free T3 were a significantly low in patients with liver cirrhosis **[16][17][18].**

In the present study, patients which are classified as child C had a higher percentage of elevated TSH levels (22.7%), decreased free T3 (15.9 %), and free T4 (9.8%) than patients classified as child A and child B. On comparing the mean serum levels of free T3 and free T4 between Child A, B, and C patients, the lowest levels were among the Child C group (2.44±0.68 & 1.16 ± 0.21, respectively) with significant differences ($P < 0.05$). When comparing the mean serum levels of TSH in Child A, B, and C patients, the highest levels observed in the Child C group (3.32±2.79), followed by the Child B group (2.85±2.04) and Child A group (2.91±1.95) but the difference was statistically not significant. The percentage of patients with high TSH, low free T3, and low free T4 increased with the progression of liver cirrhosis from child A to child C. The relationship between the severity of cirrhosis and thyroid hormones has been suggested in many previous studies **[19][20][21].**

In group A, all patients had refractory ascites and represented 50 % of included patients. 21.3 % of these patients had high TSH levels, 14.8 % had low free T3 levels and 9.8 % had low free T4 levels. The mean serum level of free T3 and free T4 was lower in the refractory ascites group than in cirrhotic patients without ascites and the difference was statically significant which indicated that the percentage of hypothyroidism could be higher in refractory ascites patients than in cirrhotic patients without ascites. We also noticed a significant relationship between increased TSH levels and lack of diuretic response ($p= 0.05$) and diuretic-induced renal impairment ($p= 0.005$) (Table 6). This indicated that hypothyroidism in cirrhotic patients with ascites could be a risk factor for refractory ascites and lack of response to diuretics. But we can't establish a causal relationship between the occurrence of refractory ascites and hypothyroidism. As patients with hypothyroidism and refractory ascites are not given medical treatment and are not followed up to see if there will be an improvement in refractory ascites or not. Further large-scale multicenter studies including patients of different geographical areas are required to evaluate thyroid functions in cirrhotic patients and the

possible relation between the occurrence of refractory ascites and hypothyroidism.

In conclusion, low serum mean level of free T3 and T4 was observed in refractory ascites patients than in cirrhotic patients without ascites. The percentage of elevated TSH levels and decreased free T3 and T4 levels was more in cirrhotic patients with refractory ascites and increase with the progression of liver cirrhosis from child A to child C. Decreased free T3 and T4 levels could be used as an indicator for advanced liver cirrhosis. Hypothyroidism could be a risk factor for the occurrence of refractory ascites in patients with advanced liver cirrhosis.

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Conflict of interest

None declared.

Ethical consideration

The permission and the official approval to carry out the study were obtained. All patients signed a written informed consent before inclusion into this study and the institutional ethical committee at Zagazig University, Faculty of Medicine approved the study (ZU-IRB #6288/10-8-2020). The study protocol conforms with the ethical guidelines of the 1975 Declaration of Helsinki.

HIGHLIGHTS

- Disturbance of thyroid functions mainly hypothyroidism was observed in patients with advanced liver cirrhosis and ascites.
- One of the possible risk factors that may lead to refractory ascites is disturbance of thyroid functions. The liver plays an important role in the metabolism of thyroid hormones
- Patients with refractory ascites carry a 1-year mortality rate about 70% and over 50% will develop hepatorenal syndrome.
- Cirrhotic patients with ascites should be monitored closely and possible factors leading to refractory ascites should be identified and treated.

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