

## Relationship Between Sleep Disordered Breathing Patterns and Liver Decompensation Among Cirrhotic Patients

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**Conflict-of-interest statement:** The authors declare that there is no conflict of interest regarding the publication of this paper.

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Received: January 31, 2020

Revised: February 23, 2020

Accepted: February 27, 2020

Published online: June 21, 2020

### ABSTRACT

**BACKGROUND AND STUDY AIM:** Liver cirrhosis is associated with different complications. There is growing evidence in the international literature about the association of liver cirrhosis with different patterns of sleep-disordered breathing (SDB). The relation between SDB and severity of liver cirrhosis is less understood. This study aimed at studying the relationship between degree of liver decompensation graded as Child class and SDB patterns in a cohort of Egyptian cirrhotic patients.

**PATIENTS AND METHODS:** Forty-eight post-viral cirrhotic pa-

tients were recruited. They were divided into three groups according to their Child class; Child A ( $n = 16$ ), Child B ( $n = 16$ ) and Child C ( $N=16$ ) groups. All patients were evaluated by through history taking, complete physical examination, and laboratory investigations. Evaluation of sleep disorders was carried out by questionnaires (Epworth sleepiness scale and Berlin questionnaire) and polysomnography.

**RESULTS:** Excessive daytime sleepiness and obstructive sleep apnea (OSA) were frequently reported among cirrhotic patients. Excessive daytime sleepiness was significantly ( $p < 0.001$ ) present in 50% of Child C group in comparison to 31.2% of Child B and 18.8% of Child A groups. In fact, not only the frequency of OSA is higher in Child class C patients but also the severity. The frequency of severe OSA was 31.8%, 12.5% and 0% among patients with Child class C, B and A respectively.

**CONCLUSIONS:** Patients with liver cirrhosis had different patterns of SDB detected by both sleep questionnaires and polysomnography. Not only the frequency of SDB but also the severity is increased with advanced stage of liver diseases.

**Key words:** Liver cirrhosis; Sleep disordered breathing; Obstructive sleep apnea; Epworth sleepiness scale; Polysomnography

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Elgammal NE, Zaher TI, ElKomy H, Emara MH, Abdallah M. Relationship Between Sleep Disordered Breathing Patterns and Liver Decompensation Among Cirrhotic Patients. *Journal of Gastroenterology and Hepatology Research* 2020; **9(3)**: 3184-3190 Available from: URL: <http://www.ghrnet.org/index.php/joghr/article/view/2790>

### INTRODUCTION

Cirrhosis is the dreaded complication of chronic liver diseases and involves loss of liver cells with irreversible scarring of the liver that impairs hepatic vasculature<sup>[1]</sup>. It is diffuse process characterized by regeneration nodules separated by dense fibrous septa causing parenchymal destruction and marked disruption of liver vasculature. Functionally, it is associated with progressive derangements of different liver functions and finally liver cell failure<sup>[2,3]</sup>.

Sleep-disordered breathing (SDB) describes many problems asso-

ciated with partial or complete stop of breathing occurring frequently at night, causing daytime sleepiness or fatigue, impairing patient performance and life. Symptoms may be gaps in breathing noticed by others, snoring and bothered sleep. Obstructive sleep apnea (OSA) is the most common form of SDB and is linked with many health hazards up to the risk of death<sup>[4]</sup>. SDB impairs daytime alertness, cognition, work and driving. Sleep apnea increases healthcare consumption<sup>[4]</sup>.

There is increasing evidence that links SDB to chronic liver diseases especially cirrhosis. However, the link of SDB to different Child classes of liver cirrhosis is controversial<sup>[5,6,7]</sup>. This study aimed at studying the relationship between degree of liver decompensation graded as Child class and sleep disordered breathing patterns in a group of Egyptian cirrhotic patients.

## PATIENTS AND METHODS

This case control study was conducted in Tropical Medicine Department Zagazig University Hospitals, Egypt and the sleep-disordered breathing unit of the Chest Department, Zagazig University Hospital and Hepatology, Gastroenterology and Infectious Diseases Department, Faculty of Medicine, Kafrelsheikh University, Kafrelsheikh, Egypt, in the period from October 2017 to June 2019.

The study was approved by the ethical review board of Zagazig University in July 2017, and a written, informed consent was obtained from each patient included in the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

**Sample size:** included 48 cirrhotic patients: Child A (16 patients), Child B (16 patients) and Child C (16 patients) according to Child's-Pugh-Turcotte score.

**Inclusion criteria:** All cirrhotic patients presented to our OPDs during the study period were offered to participate in the study.

**Exclusion criteria:** (1) Patients with any grade of hepatic encephalopathy; (2) Patients with cerebrovascular insult or with substance abuse; (3) Patients with chronic chest diseases e.g. (COPD); (4) Patients with non-viral cirrhosis; (5) Patients with renal impairment; (6) Patients with recent GIT bleeding; (7) Patients with malignancies; (8) Patients with spontaneous bacterial peritonitis (SBP); (9) Patients with hypothyroidism.

### All cases were subjected to

**1. Complete history taking with special stress on:** (1) Past history of hepatic encephalopathy; (2) Respiratory symptoms suggestive of chest disease e.g. (COPD); (3) History of drug intake and special habits (e.g. smoking, alcohol intake); (4) Sleep disturbance symptoms (excessive daytime sleepiness, insomnia at night, tiredness, difficulty waking up, snoring, choking, sleep walk, sleep talk and observed apnea that was assessed by the following: (a) **Epworth sleepiness scale (ESS) questionnaire:** used for evaluation of symptoms of increased somnolence. Eight questions, each question takes 0 to 3 scores. This scale evaluates the chance to doze off or fall asleep in the following situations: 0 = would never doze, 1 = slight chance of dozing, 2 = moderate chance of dozing and 3 = high chance of dozing. It is considered reliable if the patient's score is higher than 10<sup>[8]</sup>. (b) **Berlin questionnaire:** was used for assessment of sleep apnea in the patients. It contains 10 questions about risk factors of sleep apnea such as snoring, day time somnolence, fatigue, obesity and hypertension<sup>[9]</sup>. Patients were categorized as low risk or high risk.

**2. Detailed physical examination including:** (1) General exami-

nation & local chest and abdominal examination; (2) Body Mass Index (BMI) assessment (weight in kg / height m<sup>2</sup>).

**3. Lab investigations:** (1) CBC, liver function test, kidney function test, prothrombin time, INR, random blood sugar (RBS); (2) Viral markers and other markers whenever needed; (3) Thyroid profile (TSH, Free T3, and Free T4); (4) Arterial blood gases analysis (ABGs): Base SPO2 is the O2 before performing polysomnography while minimum SPO2 is the lowest O2 reported by polysomnography during sleep.

**4. Electrocardiography (ECG).**

**5. Imaging investigations:** Abdominal Ultrasound and Plain chest x-ray (postero- anterior view).

**6. Polysomnography (PSG):** A full-night polysomnographic sleep study was done using (SOMNO screen™ plus which is manufactured in Germany) to all patients, it is an inclusive assessment of the bio physiological variations happening while sleeping. It included electroencephalography (EEG), electrooculography (EOG), electrocardiography (ECG), Electromyography (EMG), breathing struggle (abdominal and thoracic effort), nasal and oral airflow sensors and pulse oximetry for oxygen saturation. Polysomnography screens the brain functions (EEG), heart rhythm (ECG), muscle activity (EMG) and eye movements (EOG) while the patient is sleeping<sup>[10]</sup>.

### STATISTICAL ANALYSIS

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA) and MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium). Quantitative data were expressed as the mean ± SD & median (range), and qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage). Continuous variables were checked for normality by using Shapiro Walk test. Independent samples Student's t-test was used to compare two groups of normally distributed variables while Mann Whitney U test was used for non-normally distributed variables. One Way ANOVA test was used to compare more than two groups of normally distributed variables while Kraskall Wallis H test was used for non-normally distributed variables. Post-hoc analysis for pairwise comparison was done by Tamhane's' T2 method. Categorical data were compared using Chi-square test or Fisher's exact test when appropriate. All tests were two sided. *p*-value < 0.05 was considered statistically significant (S), *p*-value < 0.001 was considered highly statistically significant (HS), and *p*-value ≥ 0.05 was considered statistically insignificant (NS).

## RESULTS

### Study patients

In this study and due to our strict exclusion criteria, we included 48 patients with post viral cirrhosis (46 HCV cirrhosis and 2 HBV cirrhosis); 16 in each Child class. Child class C are functionally deteriorated than Child B and A as shown from the data presented in Table 1 while there were no significant differences between all groups regarding the age, sex and BMI.

### Sleep questionnaire among the groups

From the data presented in Tables 2 and 3 it is obvious that cirrhotic patients had different types of sleep disorders. They had excessive daytime sleepiness and disordered Berlin questionnaire results. Note that 33.3% of cirrhotic patients in this study had excessive daytime sleepiness with 50% of this figure are patients with Child C cirrhosis. However, there were no statistically significant differences

**Table 1** Demographic and clinical data of the studied patients.

	Cirrhotic patients						Test	p-value (Sig.)
	Child A (n = 16)		Child B (n = 16)		Child C (n = 16)			
	No.	%	No.	%	No.	%		
<b>Sex</b>								
Male	9	56.20%	10	62.50%	8	50%	0.508§	0.776
Female	7	43.80%	6	37.50%	8	50%		(NS)
<b>Age (years)</b>								
Mean ± SD	48.68 ± 6.37		48.60 ± 7.36		50.81 ± 6.73		0.515*	0.601
Median (Range)	49.50 (37-58)		47.50 (37-62)		52.50 (38 - 60)			(NS)
<b>BMI (kg/m<sup>2</sup>)</b>								
Mean ± SD	25.97 ± 4.65		24.35 ± 4.50		25.94 ± 5.36		0.586*	0.561
Median	24.5		23.5		27.75			(NS)
(Range)	(18.50 - 33.50)		(17.90 - 32)		(17.80 - 34)			
Underweight	0	0%	1	6.20%	2	12.50%	4.932§	0.553
Normal weight	8	50%	9	56.20%	5	31.20%		
Overweight	5	31.20%	5	31.20%	5	31.20%		
Obese I	3	18.80%	1	6.20%	4	25%		
<b>Ascites</b>								
No ascites	14	87.50%	4	25%	0	0%	39.877§	<0.001
Mild ascites	2	12.50%	5	31.20%	1	6.20%		
Moderate ascites	0	0%	7	43.80%	10	62.50%		
Marked ascites	0	0%	0	0%	5	31.20%		
<b>Child score</b>								
Mean ± SD	5.56 ± 0.51		7.87 ± 0.88		11.12 ± 0.80		42.700~	<0.001
Median (Range)	6 (5 - 6)		8 (7 - 9)		11 (10 - 13)			(HS)

\* One Way ANOVA test, ~ Kruskal Wallis H test, § Chi-square test, p < 0.05 is significant, Sig.: significance, NS: non significant, HS: high significant.

**Table 2** Questionnaire results among the groups.

Sleep disturbance	Cirrhotic patients						Test	p-value (Sig.)
	Child A (n = 16)		Child B (n = 16)		Child C (n = 16)			
	No.	%	No.	%	No.	%		
<b>Excessive Daytime Sleepiness</b>								
Mean ± SD	4.93 ± 4.61		6.81 ± 5.56		9.68 ± 5.10		6.618~	0.037
Median	4		5.5		9.5			(S)
(Range)	(0 - 15)		(0 - 16)		(2 - 19)			
<b>Excessive Daytime Sleepiness</b>								
Absent	13	81.20%	11	68.80%	8	50%	3.442§	0.044
Present	3	18.80%	5	31.20%	8	50%		(S)
<b>Berlin questionnaire</b>								
Mean ± SD	0.50 ± 0.89		0.75 ± 1.06		1 ± 1.03		2.769~	0.251
Median	0		0		1			(NS)
(Range)	(0 - 3)		(0 - 3)		(0 - 3)			
Total score 0	11	68.80%	9	56.20%	6	37.50%	2.000§	0.157
Total score 1	3	18.80%	4	25%	6	37.50%		
Total score 2	1	6.20%	1	6.20%	2	12.50%		
Total score 3	1	6.20%	2	12.50%	2	12.50%		
<b>Sleep apnea risk</b>								
No risk	11	68.80%	9	56.20%	6	37.50%	2.483§	0.115
Low risk	3	18.80%	4	25%	6	37.50%		
High risk	2	12.50%	3	18.80%	4	25%		

~ Kruskal Wallis H test, § Chi-square test for trend, p < 0.05 is significant, Sig.: significance, S: significant, NS: non significant.

**Table 3** Post-hoc analysis for EDS among the groups

Sleep disturbance	Child A Vs Child B		Child A Vs Child C		Child B Vs Child C	
	Md±SE	p-value† (Sig.)	Md±SE	p-value† (Sig.)	Md±SE	p-value† (Sig.)
Excessive Daytime Sleepiness	-2.31 ± 0.25	< 0.001 (HS)	-5.56 ± 0.23	< 0.001 (HS)	-3.25 ± 0.29	< 0.001 (HS)

Md: Mean difference, SE: Standard error, † Tamhane T2 method, p< 0.05 is significant, Sig.: significance, HS: high significant.

between the three groups regarding scoring of Berlin questionnaire or the sleep apnea risk. It is obvious that excessive daytime sleepiness is significantly higher with advanced Child class of liver decompensation, (Table 3) Child B and C had excessive daytime sleepiness than Child A patients and Child C patients had excessive daytime sleepiness than Child B patients ( $p < 0.001$ ).

There were statistically significant relationship between excessive daytime sleepiness and hemoglobin level, Child score, serum albumin, INR and minimum SPO<sub>2</sub> while Berlin questionnaire had statistically significant correlation with minimum SPO<sub>2</sub> and base SPO<sub>2</sub> (Table 4).

**Polysomnography data among the groups**

The data obtained by sleep questionnaire is confirmed by the data obtained by polysomnography. The frequency of SDB is higher in Child class C than class B and A ( $P 0.034$ ) and consequently the prevalence of OSA and AHI were higher also in Child C than Child B and A ( $P 0.006$  and  $0.039$  respectively). However, the sleep efficacy, base SPO<sub>2</sub> and minimum SPO<sub>2</sub> were not statistically different among the groups although they were more non significantly affected in Child class C patients (Tables 5, 6).

It seems that not only the frequency but also the severity of different patterns of SDB are severe in patients with Child class C cirrhosis. Six Child A cirrhotic patients (37.5%) had OSA; 4 (25%) of them had mild OSA and 2 (12.5%) had moderate OSA and none had severe OSA. Nine Child B cirrhotic patients (56.2%) had OSA, 4 (25%) of them had mild OSA and 3 (18.8%) had moderate OSA and 2 (12.5%) had severe OSA. Twelve Child C cirrhotic patients (75%) had OSA, 4 (25%) of them had mild OSA and 3 (18.8%) had moderate OSA and 5 (31.2%) had severe OSA.

The data presented in Table 7 is of paramount importance. It seems that minimum SPO<sub>2</sub> is significantly correlated with obesity and anemia

( $P 0.043$  and  $0.039$  respectively) while AHI correlated significantly with Child score ( $P 0.043$ ) and its components (serum bilirubin, albumin). Another important correlation shown in this table is the significant correlation of Berlin questionnaire with AHI, sleep efficacy, base SPO<sub>2</sub> and minimum SPO<sub>2</sub> in comparison to excessive day time sleepiness that showed significant correlation with minimum AHI and SPO<sub>2</sub>.

**Table 4** Correlation between study parameters and sleep questionnaires

Parameters	Excessive Daytime Sleepiness		Berlin questionnaire	
	R	p-value (Sig.)	r	p-value (Sig.)
Age (years)	0.21	0.151 (NS)	-0.121	0.412 (NS)
BMI (kg/m <sup>2</sup> )	0.016	0.916 (NS)	0.002	0.992 (NS)
Child score	0.405	0.004 (S)	0.231	0.114 (NS)
Hb (g/dl)	-0.526	<0.001 (HS)	-0.134	0.365 (NS)
Total Serum Bilirubin (mg/dl)	0.308	0.033 (S)	0.227	0.12 (NS)
Albumin (g/dl)	-0.381	0.008 (S)	-0.191	0.194 (NS)
ALT (u/l)	0.157	0.287 (NS)	0.233	0.128 (NS)
INR	0.393	0.006 (S)	0.099	0.502 (NS)
pH	0.116	0.43 (NS)	0.028	0.853 (NS)
Base SPO <sub>2</sub> (%)	-0.235	0.108 (NS)	-0.294	0.042 (S)
Minimum SPO <sub>2</sub> (%)	-0.457	0.001 (S)	-0.502	<0.001 (HS)

r Spearman's rank correlation coefficient,  $p < 0.05$  is significant, Sig.: Significance, S: significant, NS: non significant, HS: high significant.

**Table 5** Polysomnography results among the groups.

Polysomnography	Cirrhotic patients						Test	p-value (Sig.)
	Child A (N=16)		Child B (N=16)		Child C (N=16)			
	No.	%	No.	%	No.	%		
<b>Sleep-disordered breathing</b>								
Absent	10	62.50%	7	43.80%	4	25%	4.476§	0.034 (S)
Present	6	37.50%	9	56.20%	12	75%		
<b>Obstructive Sleep Apnea</b>								
No OSA	10	62.50%	7	43.80%	4	25%	7.450§	0.006 (S)
Mild OSA	4	25%	4	25%	4	25%		
Moderate OSA	2	12.50%	3	18.80%	3	18.80%		
Severe OSA	0	0%	2	12.50%	5	31.20%		
<b>Apnea hypopnea index (AHI)</b>								
Mean ± SD	6.22 ± 6.32		11.55 ± 11.10		17.42 ± 13.02		6.509~	0.039 (S)
Median	3.65		8.4		14.55			
(Range)	(1.30 - 22.80)		(1.30 - 33.80)		(1.70 - 36.10)			
<b>Sleep efficacy (%)</b>								
Mean ± SD	84.95 ± 10.95		87.22 ± 10.83		83.06 ± 13.09		0.641~	0.726 (NS)
Median	88.9		88.9		87.55			
(Range)	(57.70 - 96.50)		(56.80 - 99)		(56.80 - 99.10)			
<b>Base SPO<sub>2</sub> (%)</b>								
Mean ± SD	96.25 ± 3.19		93.56 ± 3.93		95.50 ± 2.70		1.616*	0.21 (NS)
Median	96		94.5		96			
(Range)	(88 - 99)		(85 - 99)		(90 - 99)			
<b>Minimum SPO<sub>2</sub> (%)</b>								
Mean ± SD	89.56 ± 5.07		83.37 ± 9.26		81.31 ± 12.87		5.155~	0.076 (S)
(Range)	(79 - 97)		(63 - 95)		(53 - 96)			

\* One Way ANOVA test, ~ Kruskal Wallis H test, § Chi-square test for trend,  $p < 0.05$  is significant, Sig.: significance, S: significant, NS: non significant.

## DISCUSSION

The association between liver cirrhosis and SDB is increasingly reported in the literature. Sleep apnea was detected in cirrhotic patients with moderate or severe ascites. Moreover, the apnea hypopnea index (AHI) increases with more amount of ascites. Thus, an association between ascites and sleep apnea is present in cirrhotic patients<sup>[5]</sup>.

OSA was reported as a complication of hepatic decompensation<sup>[11]</sup>. OSA is 4-times higher in prevalence among cirrhotics compared to the general population<sup>[5,12]</sup>. However, the relationship between prevalence of sleep disordered breathing patterns including sleep apnea and the stage of liver cirrhosis is still under estimated and that is why we planned for carrying out this study.

Is SDB affect patients' quality of life? And the answer is yes, in

obstructive sleep apnea, patients while sleeping suffer from frequent episodes of hypoxemia occurring as a result of frequent collapse of the upper-airways leading to loud snoring, interruption of sleep, more sleep arousal and daytime sleepiness<sup>[13]</sup>, these patients frequently feel exhausted, tired and unrefreshed every morning irrespective of their sleeping time<sup>[14]</sup>.

Sleep apnea is an important deteriorating factor for cirrhotics quality of life and it seems that this quality gets more impaired with worsening of cirrhosis<sup>[15]</sup> and these findings were further emphasized by the results of this study. All cirrhotic patients in the current study had impaired sleep efficacy and although the difference among the groups was not statistically significant it seems worse in Child C patients.

We do have evidence from the current literature that management of OSA with CPAP would improve patient quality of life in patients

**Table 6** Post-hoc analysis of polysomnography among the groups

Polysomnography	Child A Vs Child B		Child A Vs Child C		Child B Vs Child C	
	Test†	p-value (Sig.)	Test†	p-value (Sig.)	Test†	p-value (Sig.)
Sleep-disordered breathing	1.129	0.288 (NS)	4.571	0.033 (S)	1.247	0.264 (NS)
Obstructive Sleep Apnea	2.729	0.435 (NS)	7.771	0.036 (S)	2.104	0.551 (NS)
	Md±SE	p-value† (Sig.)	Md ±SE	p-value† (Sig.)	Md ± SE	p-value† (Sig.)
Apnea hypopnea index (AHI)	-5.32±3.19	0.292 (NS)	-11.20 ± 3.66	0.017 (S)	-5.87 ± 4.31	0.456 (NS)

† Chi-square test,  $p < 0.05$  is significant, Sig.: significance, Md: Mean difference, SE: Standard error, S: significant, NS: non significant.

**Table 7** Correlation between study parameters and polysomnography data among the groups.

Parameters	Apnea Hypopnea index		Sleep efficacy (%)		Base SPo2 (%)		Minimum SPo2 (%)	
	r	p-value (Sig.)	r	p-value (Sig.)	R	p-value (Sig.)	r	p-value (Sig.)
Age (years)	-0.023	0.875 (NS)	-0.188	0.2 (NS)	0.057	0.699 (NS)	-0.041	0.781 (NS)
BMI (kg/m <sup>2</sup> )	0.193	0.189 (NS)	-0.187	0.203 (NS)	-0.24	0.101 (NS)	-0.293	0.043 (S)
Child score	0.374	0.009 (S)	-0.02	0.892 (NS)	-0.006	0.97 (NS)	-0.281	0.053 (NS)
Hb (g/dl)	-0.227	0.121 (NS)	0.036	0.808 (NS)	0.055	0.71 (NS)	0.299	0.039 (S)
Total Serum Bilirubin (mg/dl)	0.394	0.006 (S)	-0.013	0.928 (NS)	0.026	0.861 (NS)	-0.306	0.035 (S)
Albumin (g/dl)	-0.392	0.006 (S)	0.058	0.695 (NS)	0.03	0.841 (NS)	0.287	0.048 (S)
ALT (u/l)	0.161	0.275 (NS)	0.096	0.515 (NS)	0.002	0.99 (NS)	-0.126	0.395 (NS)
INR	0.247	0.091 (NS)	-0.035	0.813 (NS)	-0.033	0.823 (NS)	-0.182	0.216 (NS)
pH	-0.156	0.29 (NS)	-0.16	0.277 (NS)	-0.113	0.445 (NS)	0.075	0.613 (NS)
PaO2 (mmHg)	-0.103	0.486 (NS)	0.117	0.427 (NS)	0.111	0.451 (NS)	0.233	0.111 (NS)
Excessive Daytime Sleepiness	0.388	0.006 (S)	-0.119	0.419 (NS)	-0.235	0.108 (NS)	-0.457	0.001 (S)
Berlin questionnaire	0.645	<0.001 (HS)	-0.185	0.209 (NS)	-0.294	0.042 (S)	-0.502	<0.001 (HS)

S: significant, NS: non significant, HS: high significant.



with and without liver cirrhosis<sup>[16]</sup>.

The question is why SDB especially OSA were significantly more in Child C cirrhotics? And the answer can be drawn from the proposed pathogenic mechanisms of SDB among cirrhotics. Although a complex interaction between mechanical, vascular and hormonal factors seems there, still the mechanical effect is the most commonly accepted. Of particular importance is the presence of ascites and additionally the hypoalbuminemia. Hypoalbuminemia is associated with edema of the upper airway and this increases its collapsibility. This hypotonic effect of hypoalbuminemia on the upper airway muscle was proposed by other authors Ogata *et al.*, 2006. In favor of this assumption in the study conducted early by Nikania *et al* 2006 who found that early stage cirrhosis (Child A and B without ascites) is not associated with sleep disorders and OSA.

Studies reported resolution of obstructive sleep apnea after removal of ascites, supporting the theory that ascites restricts the mobility of diaphragm and decreases lung volume leading to obstructive sleep apnea. Upper airway edema occurring in cirrhotics is a second theory<sup>[11,17]</sup>.

This notion is obvious from the weighty association described in this study between Child score and serum albumin levels and sleep disorders reported by both sleep questionnaires and polysomnography among our patients.

There was statistically significant difference between Child A, Child B and Child C cirrhotic patients as regard excessive daytime sleepiness (EDS). EDS was present in 18.8% of child A group, in 31.2% of child B group and in 50% of child C group confirming the direct relationship between the severity of liver cirrhosis (represented functionally as advanced Child class) and EDS occurrence. In fact, not only the frequency of OSA is higher in Child class C patients but also the severity. The frequency of severe OSA was 31.8%, 12.5% and 0% among patients with Child class C, B and A respectively.

Ogata *et al.*, 2006 described a relationship between severe liver cirrhosis (Child C compared to Child A and B) and sleep apnea and these circumstances were associated with autonomic nervous activities and these patients had prolonged QT intervals in their ECGs exposing them to cardiac dysrhythmia. The relationship between liver disease severity and obstructive sleep apnea was described in literature<sup>[15]</sup>.

Plasma noradrenalin level is more in cirrhotic patients with ascites than that in non ascitic patients and normal individuals. Noradrenalin level at night is positively linked with obstructive sleep apnea severity and o<sub>2</sub> concentration<sup>[18]</sup>.

Bernsmeier *et al.*, 2015 described a relationship between EDS and hepatic fibrosis degree in patients NAFLD and they concluded a probable role of sleep-wake cycle regulation and eating time in the pathogenesis of nonalcoholic fatty liver disease<sup>[6]</sup>.

Pulixi *et al.*, 2014, found that non-obese patients with NAFLD had a high prevalence of OSA and this was linked with the progress of NASH (injury) and liver cirrhosis<sup>[19]</sup>.

Furthermore, identification and treatment of OSA may improve hepatic steatosis and fibrosis (measured by ultrasonography and fibrosacn) in morbidly obese patients with fatty liver<sup>[20]</sup>.

Sockalingam *et al.*, 2010 reported a very high occurrence of SDB among chronic HCV infected persons mainly in interferon therapy era<sup>[21]</sup>.

But Al Enezi *et al.*, 2017 reported no statistical difference between the stage of liver cirrhosis and both EDS and obstructive sleep apnea although they found that the risk of obstructive sleep apnea and EDS is increased among liver cirrhosis patients. Furthermore, they reported that patients with post HCV cirrhosis are more liable to EDS

and OSA. Both EDS and OSA affect Child A cirrhotics more than Child B cirrhotics. These differences from our figures are probably because their studied groups had other comorbidities such as obesity and diabetes<sup>[7]</sup>.

Another important question that we should not overlook, is there a deleterious effect of the SDB on the liver other than impairments in the quality of life? And the answer can be drawn from the scarce published literature. OSA was documented to lead to progressive impairment in hepatic condition and increased transaminases<sup>[22,23, 24,16,25]</sup>.

This study had its potential limitations. First, it is a single center study. Second, the small number of patients recruited. Third, lack of long-term follow up. Fourth, lack of reevaluation of the liver conditions after treatment of the reported SDB patterns e.g. OSA with CPAP. Future, large scale studies may probably overcome the limitations of the current study and answer many of the unanswered questions.

In conclusion, patients with liver cirrhosis had different patterns of SDB detected by both sleep questionnaires and polysomnography. Not only the frequency of SDB but also the severity is increased with advanced stage of liver diseases.

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