Indian J Otolaryngol Head Neck Surg
(November 2019) 71(Suppl 3):S1679–S1682; DOI 10.1007/s12070-015-0914-8

ORIGINAL ARTICLE

# Evaluation of Liver Functions Based on Serum Aminotransferase Enzyme Levels in Patients with Obstructive Sleep Apnea Syndrome

**Doğan Atan[1] · Sabri Köseoğlu[2] · Kürşat Murat Özcan[1] · Aykut İkincioğulları[1] · Ayşe Betül Topak[1] · İbrahim Özcan[3] · Hüseyin Dere[1]**

Received: 8 April 2015 / Accepted: 16 September 2015 / Published online: 22 September 2015


**Abstract** Obstructive sleep apnea syndrome (OSAS) is associated with fatty liver disease. In the present study, relations between alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels and the severity of OSAS and polysomnography parameters were investigated. The study included 194 patients with OSAS and 114 control patients. The patients underwent an overnight polysomnography (PSG) in the Sleep Laboratory. ALT and AST levels were compared between the patients and the controls and between the subgroups of the patients. ALT and AST levels were also compared with the PSG parameters REM AHI, NREM AHI and minimum $O_2$ saturation separately. The mean ALT was 28.95 in the patients and 17.85 in the controls ($p < 0.001$) with a statistically significant difference and the mean AST was 23.62 in the patients and 16.53 in the controls with a statistically significant difference ($p < 0.001$). The patients with OSAS had significantly higher ALT and AST levels. The higher the ALT and AST levels were, the more severe the disease was, though the differences between the subgroups of the patients were not significant.

**Keywords** Sleep apnea · Aspartate aminotransferase · Alanine aminotransferase · Polysomnography

## Introduction

Non-alcoholic fatty liver disease (NAFLD) refers to deposition of fatty acids in the liver cells without inflammation [1]. The diagnosis of NAFLD is confirmed by liver biopsy; however, an asymptomatic increase in serum aminotransferase levels is the first sign of the disease [2]. NAFLD, obstructive sleep apnea syndrome (OSAS) and metabolic syndrome are interrelated. Metabolic syndrome, characterized by obesity, causes NAFLD and OSAS [3]. Dyslipidemia which develops in metabolic syndrome and hyperglycemia and which can be due to insulin resistance leads to deposition of fatty acids in the liver, which results in an increase in serum aminotransferase levels [4]. NAFLD appears in 10–24 % of the normal population; however, it appears in 57–74 % of the obese population [4]. Central obesity affects the upper respiratory tract opening and compliance through fat deposition around the upper respiratory tract and the respiratory pattern through abdominal fat deposition, both of which increase the tendency to develop OSAS. Seventy percent of the cases of OSAS are obese and the incidence of OSAS in obese females and males is 40 % [5].

During hypoxemic periods in sleep apnea, oxidative stress occurs, which results in changes in the liver which in turn progress into liver fibrosis in NAFLD [6]. In a study by Tanne et al. [7] OSAS and the degree of OSAS were reported to be risk factors for increases in serum aminotransferase enzymes. The aim of the current study was to investigate relations between increased serum aminotransferase levels and OSAS, the degree of OSAS and polysomnography parameters.

✉ Doğan Atan
doganatan@gmail.com

[1] Ankara Numune Education and Research Hospital, Samanpazarı, Ankara, Turkey

[2] Tarsus State Hospital, Mersin, Turkey

[3] Kayseri Education and Research Hospital, Kayseri, Turkey

## Methods

The study was conducted at Ankara Numune Education and Research Hospital between January 2008 and January 2014. A hundred and ninety-four patients presenting with witnessed apnea, extreme sleepiness and snoring underwent overnight polysomnography (PSG). Following PSG, fasting peripheral venous blood specimens were taken to measure serum aminotransferase (ALT and AST) levels with the Sysmex WE-2100 (Sysmex, the USA).The patients were divided into three groups based on the apnea-hypopnea index (AHI). The AHI scores of 5–15 indicated mild OSAS, the AHI scores of 15–30 indicated moderate OSAS and the AHI scores of >30 indicated severe OSAS. The patients with chronic liver disease, cardiovascular disease, chronic lung disease, chronic renal disease and body mass index >40 and those taking >20 g/day of alcohol were not included into the study. A hundred and fourteen patients similar to the patient group in terms of age, gender and other demographic features were assigned into the control group. The people assigned into the control group did not have complaints of sleep apnea, hypertension, diabetes, chronic lung disease, cardiovascular disease, chronic renal disease or body mass index >40 or take >20 g/day of alcohol. Fasting peripheral venous blood specimens were also taken from the control patients to determine serum AST and ALT levels.

### Polysomnography

The patients underwent overnight polysomnography under the supervision of a technician while having their spontaneous sleep alone in a room in the Sleep Lab of Ankara Numune Education and Research Hospital. Both voice- and video-recordings were performed overnight. Polysomnography was performed with Alice 5 PSG device. On PSG, four channels electroencephalography (EEG), electromyography (EMG-submental), electromyogram (EMG-right-left tibialis), two channels electrooculogram (right-left EOG) and electrocardiography (ECG) were performed and nasal air flow, thoracic and abdominal respiratory movements, oxygen saturation with pulse oximetry and data about body positions were recorded. Data were manually scored and AHI, REM-AHI, Non-REM-AHI and minimum oxygen saturation were recorded.

ALT and AST levels were compared between the patients and the controls and between the subgroups of the patients based on AHI scores. In addition, ALT and AST levels were compared with the PSG parameters AHI, REM AHI, NREM AHI and minimum $O_2$ saturation separately.

### Statistical Analyses

Continuous variables were expressed in ±SD. Categorical variables were expressed in percentages. Kolmogorov–Smirnov test was used to determine whether the data were normally distributed. Student's t test was used to determine differences between the groups in normally distributed data and Mann–Whitney U test was used determine differences between the groups in the data not distributed normally. Chi-square test was utilized to determine differences between the groups in categorical variables. Pearson correlation analysis was made to determine the relations between the variables. $p < 0.05$ was considered significant. Statistical analyses were made with Statistical Package Program for Social Sciences for Windows version 21.0 (SPSS Inc., Chicago, IL, USA).

## Results

There were 143 males (73.7 %) and 51 females (26.3 %) in the patient group and 80 males (70.2 %) and 34 females (29.8 %) in the control group without a statistically significant difference ($p = 0.509$). The mean age of the patient group was 48.53 ± 9.94 years and the mean age of the control group was 47.45 ± 10.87 years without a statistically significant difference ($p = 0.389$) (Table 1).

Of 194 patients, 70 had mild OSAS (36 %), 33 had moderate OSAS (17 %) and 91 had severe OSAS (47 %) based on the apne-hypopnea index (AHI) (Table 2).

The mean ALT levels were 28.95 ± 16.78 in the patient group and 17.85 ± 5.42 in the control group. The patients had statistically significantly higher ALT levels ($p < 0.001$). The mean AST levels were 23.62 ± 8.62 in the patient group and 16.23 ± 5.28 in the control group.

**Table 1** The distribution of the patient and control groups by age and gender

| Age | Patients | Controls | *p* |
|---|---|---|---|
| Gender | 48.53 ± 9.94 | 47.45 ± 10.87 | 0.389 |
| Male | 143 | 80 | 0.509 |
| Female | 51 | 34 | |

**Table 2** The distribution of patients by the severity of OSAS

| Severity of OSAS | AHI scores | Number of patients (n) | % |
|---|---|---|---|
| Mild OSAS | 5–15 | 70 | 36 |
| Moderate OSAS | 15–30 | 33 | 17 |
| Severe OSAS | >30 | 91 | 47 |

**Table 3** A comparison of the mean ALT and AST levels between the patients and the controls

| | Patients | Controls | *p* |
|---|---|---|---|
| ALT | 28.95 ± 16.78 | 17.85 ± 5.42 | <0.001 |
| AST | 23.62 ± 8.62 | 16.23 ± 5.28 | <0.001 |

**Table 4** The relations between PSG parameters and ALT and AST levels

| PSG parameters | Mean values | *p* (for ALT) | *p* (for AST) |
|---|---|---|---|
| AHI | 35.19 ± 26.58 | 0.065 | 0.060 |
| REM AHI | 34.52 ± 28.35 | 0.056 | 0.054 |
| NREM AHI | 39.11 ± 24.04 | 0.080 | 0.058 |
| Minimum $O_2$ saturation | 75.40 ± 14.64 | 0.023 | 0.006 |

The patients had significantly higher AST levels ($p < 0.001$) (Table 3).

As for the patient subgroups classified based on AHI scores, the mean ALT levels were 26.35 ± 18.21 in the patients with mild OSAS, 29.33 ± 19.90 in the patients with moderate OSAS and 30.82 ± 14.13 in the patients with severe OSAS. The mean AST levels were 21.81 ± 6.60 in the patients with mild OSAS, 24 ± 8.65 in the patients with moderate OSAS and 24.87 ± 9.73 in the patients with severe OSAS. The differences in the mean ALT and AST levels were not statistically significant between the patients with mild OSAS and those with moderate OSAS ($p = 0.470$, $p = 0.205$). The patients with severe OSAS and those with mild OSAS also did not statistically significantly differ in the mean ALT and AST levels ($p = 0.092$, $p = 0.019$). The patients with moderate OSAS and those with severe OSAS did not statistically significantly differ in the mean ALT and AST levels, either ($p = 0.694$, $p = 0.631$).

The PSG parameters AHI, REM AHI and NREM AHI had a positive correlation with ALT and AST levels. As ALT and AST levels increased, so did AHI scores, though the changes were not statistically significant. The minimum oxygen saturation had a negative correlation with ALT and AST levels. While the minimum oxygen saturation decreased, ALT and AST levels increased. Minimum oxygen saturation was significantly correlated with AST ($p = 0.006$), and ALT ($p = 0.023$) though the other changes were not statistically significant (Table 4).

## Discussion

Obstructive sleep apnea syndrome (OSAS) most frequently appears in people aged 40–65 years and the incidence of OSAS decreases after the age of 65 years [8]. The mean age of the patients included into the present study was 48.53 years, which is consistent with that reported in the literature. In a study by Young et al. [9] the prevalence of sleep related breathing disorders was 9 % in females and 24 % in males, both of whom had AHI scores of >5. The patients included into the present study had AHI scores of >5 and a higher rate of the male patients had OSAS, which is congruent with the literature.

Compared to the general population, a higher rate of the patients with OSAS has collapse of the upper respiratory tract and a higher negative inspiratory pressure due to decreased muscle tone. Partial and total obstructions of the upper respiratory tract result in snoring and obstructive apnea during sleep [10]. As a result of apnea and hypopnea, hypoxemia occurs, which causes oxidative stress and in turn tissue and organ damages. There have been two hypotheses proposed to explain NAFLD. The first hypothesis is that damage to hepatocytes occurs due to insulin resistance. The other one is that hepatocytes are damaged by oxidative stress [11]. In the current study, insulin resistance and diabetes were not investigated. It would be more useful to perform tests to determine insulin resistance and diabetes in further studies. Changes in AST and ALT values in OSAS patients were examined as these changes were thought to be an indicator of NAFDL. Radiological examinations, liver biopsy and tests for insulin resistance and inflammatory mediators were not performed to diagnose NAFDL since this study focused on evaluation of liver enzyme values in OSAS patients. Relationships of these enzymes with NAFDL and OSAS should be investigated with other diagnostic tests in further studies.

Daltro et al. [12] found that patients with OSAS had higher ALT and AST levels than those without OSAS. In addition, Byrne et al. [13] reported that ALT and AST levels were higher in patients with OSAS than those without OSAS. In the current study, the mean ALT and AST levels were 28.95 ± 16.78 and 23.62 ± 8.62 in the patients with OSAS respectively. The differences in the mean ALT and AST levels between the patients and the controls were significant, which is consistent with the literature.

In the current study, the relation between the severity of OSAS and ALT and AST levels was also investigated. As ALT and ALT levels increased so did the severity of the disease, though the differences were not significant. These high levels of ALT and AST might have been caused by an increase in oxidative stress in the liver due to prolonged hypoxemia periods. The role of apnea and hypopnea periods in duration of hypoxemia is as important as AHI scores. Further studies could focus on relations between apnea and hypopnea periods and serum aminotransferase levels. Prolonged apnea and hypopnea lead to longer

durations of hypoxemia which may increase oxidative stress in the liver.

In a study by Norman et al. [14] as the polysomnography parameters, minimum oxygen saturation and <90 % oxygen saturation decreased, ALT and AST levels increased and the changes were statistically significant. The present study also showed a negative relation between minimum oxygen saturation and ALT and AST levels, though it was not statistically significant. In addition, ALT and AST levels had a positive correlation with AHI, REM AHI and Non-REM; however, it was not statistically significant. In fact, studies with larger sample sizes could provide more reliable results about these relations.

The findings of this study showed that levels of serum aminotransferase enzymes were significantly higher in the patients with OSAS than in the controls and that as the severity of the disease increased so did ALT and AST levels. It can be concluded that OSAS affects liver functions.

**Compliance with Ethical Standards**

**Conflict of interest** There are no conflicts of interest.

## References


1. Türkay C, Ozol D, Kasapoğlu B, Kirbaş I, Yıldırım Z, Yiğitoğlu R (2012) Influence of obstructive sleep apnea on fatty liver disease: role of chronic intermittent hypoxia. Respir Care 57:244–249
2. Lee RG (1989) Nonalcoholic steatohepatitis: a study of 49 patients. Hum Pathol 20:594–598
3. Vgontzas AN, Bixler EO, Chrousos GP (2005) Sleep apnea is a manifestation of the metabolic syndrome. Sleep Med Rev 9:211–224
4. Sass DA, Chang P, Chopra KB (2005) Nonalcoholic fatty liver disease: a clinical review. Dig Dis Sci 50:171–180
5. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP (2010) Pathophysiology of sleep apnea. Physiol Rev 90:47–112
6. Kohler M, Stradling JR (2010) Mechanisms of vascular damage in obstructive sleep apnea. Nat Rev Cardiol 7:677–685
7. Tanné F, Gagnadoux F, Chazouillères O et al (2005) Chronic liver injury during obstructive sleep apnea. Hepatology 41:1290–1296
8. McNamara SG, Grunstein RR, Sullivan CE (1993) Obstructive sleep apnea. Thorax 48:754–764
9. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 328:1230–1235
10. Greene JS, Zipfel TE, Harlor M (2004) The effect of uvulopalatopharyngoplasty on the nasality of voice. J Voice 18:423–430
11. Day CP, Saksena S (2002) Non-alcoholic steatohepatitis: definitions and pathogenesis. J Gastroenterol Hepatol 17:377–384
12. Daltro C, Cotrim HP, Alves E et al (2010) Nonalcoholic fatty liver disease associated with obstructive sleep apnea: just a coincidence? Obes Surg 20:1536–1543
13. Byrne TJ, Parish JM, Somers V, Aqel BA, Rakela J (2012) Evidence for liver injury in the setting of obstructive sleep apnea. Ann Hepatol 11:228–231
14. Norman D, Bardwell WA, Arosemena F et al (2008) Serum aminotransferase levels are associated with markers of hypoxia in patients with obstructive sleep apnea. Sleep 31:121–126