

## An Investigation of the Relationship between Non-Alcoholic Fatty Liver and Corticosteroid Use

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### ABSTRACT

**BACKGROUND AND OBJECTIVE:** The prevalence of non-alcoholic fatty liver is one of the major health problems in the society, which is mainly caused by obesity and the use of certain drugs. The aim of this study is to evaluate the relationship between non-alcoholic fatty liver and corticosteroid use.

**METHODS:** This case-control study was performed on 76 patients with normal BMI in two groups of 38 (with or without non-alcoholic fatty liver). The groups were matched according to age and gender and were compared regarding at least 6 months of corticosteroid use and suffering from non-alcoholic fatty liver.

**FINDINGS:** Of 76 patients who were included in the study, 51 (65.4%) were male. 26% (20 people) of the case group and only 3.9% (3 people) of the control group used corticosteroid. The results showed significant effect of corticosteroid on fatty liver disease ( $p < 0.001$ ). In addition, the two variables of gender and corticosteroid use could predict 32% of changes in fatty liver. In this study, odds ratio in men was almost 6 times higher than women (CI-95%: 2.04–17.54, OR=5.92) ( $p < 0.001$ ). The odds ratio of developing fatty liver disease in the corticosteroid group was almost 13% higher than those who did not use corticosteroid (CI-95%: 3.94 – 49.51, OR = 12.96).

**CONCLUSION:** The results of this study showed that the effect of corticosteroid use on the fatty liver, especially among men, is significant.

**KEY WORDS:** *Non-Alcoholic Fatty Liver Disease, Corticosteroid, Weight.*

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## Introduction

**N**on-Alcoholic Fatty Liver Disease (NAFLD) occurs due to fat deposits in the cytoplasm of liver cells (1, 3). The prevalence of this disease is about 25 – 30%, and affects more than 50% of patients with diabetes and obesity (4). The prevalence of this disease was reported to be 1.7–9.2% in Iran (5).

The mechanism of this disease is characterized by resistance to insulin and the entrance of free fatty acids into the liver cells (6, 7). One study found that the use of chemotherapy drugs (methotrexate), antiarrhythmic drugs (amiodarone), and nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids may cause fatty liver disease (4). However, in another study, the results indicated that the chemotherapy drugs are ineffective in fatty liver disease (8).

Glucocorticoids a group of corticosteroids that have potent anti-inflammatory properties. Corticosteroid therapy is associated with several types of liver damage, some due to the exacerbation of basic liver disease and some others are directly caused by corticosteroid therapy (9). A study has reported the prescription of glucocorticoids to be 25.73% in Iran. In addition, statistics show that on average, from every four to five prescriptions, one prescription contains dexamethasone (10). The side effects of these drugs include increased appetite (11) and increased free fatty acids in the liver. This fat is more absorbed by the peripheral tissue and is less than the food, which can be a factor for exacerbation and development of non – alcoholic fatty liver disease in patients who take corticosteroids (4). In this regard, one can refer to the studies by Wang et al. and Auer et al. who reported that corticosteroid use was effective in developing non – alcoholic fatty liver disease (12, 13).

However, in the study by Chen et al., dexamethasone was not associated with damage to liver cells (14). Considering the controversial results in this regard, and on the other hand, the increase in the incidence of corticosteroid use and high prevalence of fatty liver, the present study was conducted to determine the association between consumption of corticosteroids and non – alcoholic fatty liver in patients who referred to Khatam al-Anbia Hospital in Shushtar in 2018.

## Methods

This case-control study was conducted in 2018 after approval by the Ethics Committee of Shushtar University of Medical Sciences with the code of ethics IR.AJUMS.REC.1397.407. According to similar studies (15), 76 hospitalized patients with normal BMI and non – alcoholic fatty liver disease were randomly selected from the wards of Khatam al-Anbia Hospital in Shushtar and were divided into two groups of case and control (38 people in each group). The groups were matched in terms of age and gender, and were studied after obtaining written informed consent for at least six month of corticosteroid use in two oral and injectable forms.

Data were collected using a researcher-made questionnaire that included questions about demographic information and the use of betamethasone, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone and triamcinolone and clobetasol (10, 12). To determine the validity of the instrument, a questionnaire was provided to 10 faculty members and internists to examine in terms of content and usage. Diagnosis of fatty liver in patients was done by ultrasound and based on increased liver echogenicity at ultrasound examination and was divided into four groups of healthy, mild (Grade 1), moderate (Grade 2) and severe (Grade 3) fatty liver and ultrasound result was attached to patient's records (15).

Collected data were analyzed by Kolmogorov-Smirnov, Chi-square, Fisher's test, logistic regression and t-test using SPSS 16 software.  $P < 0.05$  was considered significant.

## Results

The mean age of patients was  $40.28 \pm 12.06$  years. The mean age in subjects with fatty liver in case group who consumed corticosteroids ( $37.28 \pm 2.5$ ) was lower than those who did not consume corticosteroids ( $39.8 \pm 3.06$  years). In this study, 20 subjects (26%) in the case group and 3 subjects (3.9%) in the control group used corticosteroids, indicating the significant effect of corticosteroid on fatty liver disease ( $p < 0.001$ ).

Of the eight different corticosteroid drugs, only four types were used by patients so that the highest & lowest frequencies were significantly related to oral prednisolone (17 cases (21.8%)) as well as hydrocortisone and betamethasone ampoules (each in one case (1.3%)), respectively. Based on the logistic regression test, two variables of gender and corticosteroid consumption can predict 32% of the changes in developing or not developing of fatty liver disease. The odds ratio of developing fatty liver disease in the corticosteroid group was almost 13% higher than those who did not use corticosteroid (CI-95%: 3.94–49.51, OR=12.96). In addition, odds ratio in men was almost 6 times higher than women (CI-95%: 2.04–17.54, OR=5.92).

There was no statistically significant relationship between the underlying diseases (diabetes, hypertension and hyperlipidemia) and fatty liver (Table 1).

**Table 1. Contingency table for demographic information in case and control groups**

Group		Case N(%)	Control N(%)	P-value
Diabetes	Yes	10(13.2)	7(9.2)	0.583
	No	28(36.8)	31(40.8)	
Hypertension	Yes	5(6.6)	2(2.6)	0.430
	No	33(43.4)	36(47.4)	
Hyperlipidemia	Yes	5(6.6)	2(2.6)	0.430
	No	33(43.4)	36(47.4)	
Gender	Woman	6(7.9)	20(26.3)	<0.001**
	Man	32(42.1)	18(23.7)	

\* Significance at the level of 0.05; \*\* significance at the level of 0.01

## Discussion

The results of this study indicate the relationship between corticosteroid use and non-alcoholic fatty liver disease in patients, which is consistent with the results of studies by Rabinovich et al., Wang et al., and Auer et al. (4, 12, 13), but is not consistent with the studies by Chen et al. and Gomez Dumm et al. (14, 16). According to the results of these studies, cortisone use can disrupt metabolic pathways and cause fat accumulation in the kidneys. The reason for this difference with the present

study it can be attributed to the fact that in these studies, the samples were subject to a low-fat and low-sugar diet that might affect the results. In addition, the present study showed that two variables of corticosteroid use and male gender can predict 32% of changes in fatty liver, which is consistent with the studies of Orangi et al. (17) and Auer et al. (13). That's because the mass of fat in the body of men is more than women (17). However, many studies has shown that the odds ratio of women for developing fatty liver in the presence of polycystic ovarian syndrome is more than men (6). In this study, the mean age of patients using corticosteroids was lower in case group compared to those who did not use corticosteroids.

As the age increases, the reduced ability of the liver to decompose fatty acids causes fat accumulation and inflammation in the liver (7); perhaps the reason for inconsistency between the present study and some other studies is the fact that in the present study, the use of corticosteroids has led to fatty liver disease at an early age in the patients. The most commonly used drug in the present study was prednisolone, which is consistent with the study by Wang et al. (12); however, hydrocortisone in the study by Auer et al., (13), and dexamethasone in the studies by Brenner et al., and Chen et al. has been reported as the most commonly used drug (14, 18).

The reason for inconsistency in the type of drug can be associated with the type of disorder in patients, type of diet, and underlying disease, such as insulin resistance and obesity (14). The present study showed that corticosteroid use has an effect on developing fatty liver. Considering the complications of the disease and drugs, it is suggested that a healthy diet, weight loss with exercise, and modification in the use of corticosteroids should be considered as front line therapy for these patients.

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