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Peer Review Report for "Comparison of Body Mass Index, Smoking, Vitamin E and Type of Oil Consumed between Patients Suffering from Non-alcoholic Fatty Liver Disease versus Non-affected Patients: A Case-Control Study"

Author(s): Mehran Naghibeiranvand, Atefeh Visskaramian, Fatemeh Mehrabirad, Zahra Mohammadi

Review Timeline:

Submit Date:	22 Aug 2020
Revised Date:	29 Nov 2020
Accepted Date:	29 Nov 2020

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | Revision (0)

28 Aug 2020

Dear AE,
Comments for the authors:
- Provide in the abstract an informative and balanced summary of what was done and what was found to be suitable.
- Describe the setting, locations, and relevant dates, all statistical methods, was completed.
- Type of oil consumed in Table 3 Type in English.
- The adequacy of the studied sample is not well expressed.
- In the results, the descriptive data and the results obtained are well expressed.
- The conclusion is justified and acceptable.
- Study limitations are not stated.
- The overall interpretation of the results is appropriate taking into account the objectives, analyzes, results of similar studies, and other related evidence.
Thanks.

REFEREE: Reviewer | **Revision** (0) 17 Oct 2020

Dear AE,
Thanks for submitting this manuscript to the JJCDC. There are some comments in my opinion for the authors to the article: Comparison of Body Mass Index (BMI), smoking, taking vitamin E and type of oil consumed by patients suffering from nonalcoholic fatty liver Disease with nonaffected patients (A case-control study) ‘
Thank you for the opportunity to revise this study.
1- Title:
Suggestion: revise your title.
Comparison of Body Mass Index (BMI), smoking, taking vitamin E and type of oil consumed between patients suffering from nonalcoholic fatty liver Disease versus nonaffected patients: A case-control study
2- Introduction
Divide the introduction into some paragraphs.
3- Method
a) Mention year of study in the method section
b) Write method section in the different subheadings such as setting and sample; data collection; instruments; ethic; data analysis
c) Participants were randomly divided into case and control groups??????? What???? Randomly?????? This study is case-control. You can't use random. ????
4- Results
table 3 is Persian. Revise.
Write discussion in some paragraphs.
Mention study limitation.
Mention suggestions for future studies on the basis of your results.
Suggestion: use this reference: The Prevalence of Non-Alcoholic Fatty Liver Disease Among Patients With and Without Coronary Artery Disease [Seyed Jalal Hashemi]
Best regards

REFEREE: Associate Editor | **Revision** (0) 17 Oct 2020

Dear EIC,
Thanks to the authors for submitting your manuscript in JJCDC. This study is interesting in the chronic illness field. Based on our reviewers' comments this article needs some revisions in all parts. I recommend them to revise the manuscript and turn it back as soon as possible.
With regards.

REFEREE: EIC | **Revision** (0) 17 Oct 2020

Dear author,
Thank you for submitting your manuscript in JJCDC. Based on our reviewers' comments your article needs some revisions in all parts of it. I recommend you revise manuscript and turn back as soon as.
With regards.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Comparison of Body Mass Index (BMI), smoking, vitamin E and type of oil consumed between patients suffering from non-alcoholic fatty liver disease versus non affected Patients: a case-control study

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Abstract:

Background: Non-alcoholic fatty liver disease has an increasing trend in the world and if left untreated can lead to liver failure and death. Lifestyle modification is very important in the treatment of this disease.

Objective: The aim of this study was to determine the comparison of body mass index, smoking, vitamin E consumption and type of oil consumed by patients with non-alcoholic fatty liver disease with non-alcoholic patients.

Patients and Methods: The present study was a retrospective case-control study that was performed on 120 patients referred to the ultrasound unit of Nomadic Martyrs Hospital in Khorramabad. Participants were divided into two groups: case (61 people) and control (59 people). The questionnaire used consisted of three parts: the first part was related to demographic information, the second part was related to liver ultrasound answer and the third part was related to Height, weight, BMI, weekly vitamin E intake, daily smoking status and type of oil consumed. Data analysis was performed using SPSS-23 software and descriptive and inferential statistical methods.

Results: Most of the participants in the study were 69 (55.8%) and 92 (76.66%) were married. The mean BMI of patients with non-alcoholic fatty liver disease was significantly higher than non-alcoholic patients (P = 0.003). There was no statistically significant difference in daily smoking and weekly intake of vitamin E in patients with and without non-alcoholic fatty liver disease (P <0.05). According to Fisher's exact test, it was found that there was a statistically significant difference in the frequency distribution of the type of oil consumed by patients with non-alcoholic and non-alcoholic fatty liver (P = 0.014). Also, a statistically significant difference was observed in the frequency distribution of the type of oil consumed by patients with non-alcoholic and non-alcoholic fatty liver (P = 0.014).

Conclusion: Consumption of olive and sesame oil along with weight loss is recommended. Smoking as a risk factor, as well as the use of vitamin E to prevent and treat non-alcoholic fatty liver disease, requires further studies with a larger sample size.

Keywords: Non-alcoholic fatty liver, Body mass index, Obesity, Smoking, Vitamin E, Fatty acids.

1. Background:

Nonalcoholic fatty liver disease as one of the most common non-communicable diseases in developed countries has affected about 20% to 30% of the adult population. This rate reaches up to 80% in fat people (1). Incidence of fatty liver is expected to increase in the future (2). In Asia, the prevalence of this disease varies between 12% to 24% by age, sex, place of residence and people race. In the general population of Iran, the prevalence of NAFLD varies between 2/9% to 1/7%, which is 55/6% in patients suffering from diabetes type 2 (3). To define NAFLD disease, there should be some evidence of liver steatosis, or by imaging, histology and the absence of secondary factors for collecting the liver fat such as high alcohol consumption, long term use of osteotogenic drugs or hormonal disorders (4). The significance of NAFLD is due to the destruction of liver cells which began with a wide spectrum of liver steatosis, and in the absence of early diagnosis and proper treatment, it can lead to an advanced and irreversible liver disease called Cirrhosis (5), nonalcoholic steatohepatitis, fibrosis, and even liver cancer which its treatment is liver transplantation (6).

The most common cause of death in patients suffering from NAFLD is cardiovascular disease. Liver biopsy is a gold standard to describe liver tissue changes in NAFLD patients. NAFLD management should include liver disease treatment as well as metabolic related compounds such as obesity, hyperlipidemia and diabetes. According to various studies, the high prevalence of NAFLD is associated with an epidemic obesity and inertia. Increasing inactive periods can have a potential role in development or incidence of fatty liver (7). For this reason, treatment of this disease mainly focused on behavioral change and life style interventions including diet, increasing physical activity and weight loss (8, 9).

Dehghan et al showed in their study that most patients suffering from fatty liver have moderate physical activity; therefore, they recommend life style changes and physical activity interventions along with a diet to ameliorate fatty liver (10). Among the risk factors of the incidence of this disease, the relationship between nutritional habits and the incidence of this disease has been proven in various studies (11). In all patients, the use of natural antioxidants such as fruits and vitamins C and E is effective under physician supervision (12). Vitamin E is located in the adipose layer of the cell wall and in the cell, preventing cell wall destruction. This vitamin is the most important factor for having a strong immune system, healthy skin and eyes but still all its benefits and risks are not well known (13). Saturated fatty acids have only one carbon to carbon chain in the hydrocarbon column. These facts cause the hypothalamus inflammation and lead to metabolic complications such as obesity (14).

Tran's fatty acids in food stuffs are produced due to bacterial metabolism (dairy products) and hydrogenation (margarine) and may play a role in NAFLD (15). Cigarette smoking has been clearly identified as a risk factor for hepatocellular carcinoma, and accelerates the process of chronic liver disease including liver hepatitis A and C and biliary insufficiency (16). The results of a study by Jung et al (2019) showed that smoking in Korean men, women and the elderly contributes to the development of NAFLD (17). Also, the results of Liu et al study (2013) which was conducted on 2961 Chinese people showed that those people who smoke very much and burn more than 40 cigarettes per day are more likely to have NAFLD than nonsmokers (18). Due to the increasing increase of non-alcoholic fatty liver in most communities, including Iran, and also considering that this disease can be prevented and treated, and if left untreated leads to liver failure and carries the risk of death.

2. Objective:

The aim was to compare body mass index, smoking, vitamin E consumption and type of oil consumed by patients with non-alcoholic fatty liver disease with non-alcoholic patients.

3. Patients and Methods:

3.1. Setting and sample

The present study was a retrospective case study in which 120 patients referred to the ultrasound unit of Ashayer Shohaday Hospital affiliated to Lorestan University of Medical Sciences in 2018 were studied. Participants were Non-random divided into case (n = 61) and control (n = 59) groups. Inclusion criteria included: complete satisfaction to participate in the study, age between 18-65 years and having a written report of liver ultrasound and exclusion criteria included: alcohol users, pregnant women, patients undergoing Chemotherapy, patients with hepatic impairment, hepatitis B and C, patients with renal failure and on dialysis, patients with heart failure, thyroid disease, hemochromatosis, pancreatitis and Cushing's syndrome. After receiving the license from the Islamic Azad University of Khorramabad Branch and receiving the code of ethics and the necessary coordination with the officials of the hospital in question, the research began. The researchers were present in the ultrasound unit for 12 days and after performing liver ultrasound in the patients referred, those who met the inclusion criteria were included in the study. It should be noted that the diagnosis of fatty liver was made based on a written ultrasound report. The questionnaires were completed by the patients and if the patient was not able to fill in the questionnaire, the researchers asked the questions orally and entered them into the questionnaire.

3.2 Instruments

Data collection tools included a three-part questionnaire. The first part was about the demographic characteristics of gender, age, education, marital status, economic status and place of residence. The second part is related to the written answer of liver ultrasound (non-alcoholic fatty liver disease was considered regardless of its grade) and the third part is related to questions about height, weight, BMI, vitamin E consumption per week, smoking status per day and It was oil consumption.

3.3 Data analysis

In order to analyze the data, SPSS-23 software and descriptive statistical methods of frequency, percentage, mean and standard deviation were used. Also, in order to compare the variables in the case and control groups, independent t-test, Mann-Whitney test and Fisher's exact test were used. Significant level was considered 0.05.

4. Results: In this study, 120 patients referred to the ultrasound ward of Khorramabad Nomadic Martyrs Hospital were examined, of which 61 were in the case group and 59 were in the control group. Of the total patients participating in the study, 51 (44.2%) were male and

69 (55.8%) were female. There was no statistically significant difference in the frequency distribution of patients with non-alcoholic fatty liver disease by sex (P = 0.9830). The mean age of participants in the case group was 44.11 (age range 18-65 years) and in the control group was 39.12 (age range 23-65 years). Most of the research units were 82 people (68.33%) in terms of education at the undergraduate and postgraduate level. There was no statistically significant difference in the frequency distribution of patients with non-alcoholic and non-alcoholic fatty liver disease (P <0.05). Also, 28 (23.3%) of the participants were single and 92 (76.7%) were married. There was no statistically significant difference in the frequency distribution of patients with fatty liver and non-fatty liver (P> 0.05). There was no statistically significant difference in the frequency distribution of patients with non-alcoholic and non-alcoholic fatty liver disease (P <0.05) **(Table 1).**

Table 1.Comparison of demographic characteristics of patients with non-alcoholic and non-alcoholic fatty liver

Variable		Nonalcoholic fatty liver patients	No affected with Nonalcoholic fatty liver patients
Sex	Male Female	23(37/7%) 38(62/3%)	(47/4%)28 (52/55%)31
Educational status	Diploma And Under diploma BA MA	46(75/5%) 11(18/03%) 4(6/55%)	36(61%) 12(20/35%) 11(18/65%)
Marital status	Single Married	9(14/7%) 52(85/3%)	19(32/20%) 40(67/80%)
economic status	Excellent Good medium Weak	14(22/90%) 17(28%) 23(37/60%) 7(11/50%)	11(18/70%) 13(22%) 26(44%) 9(15/30%)

In patients with non-alcoholic fatty liver, the mean and standard deviation of BMI was 29.33± 4 4.01 and in non-alcoholic patients, the mean and standard deviation of BMI was 24.9±3.02. The mean BMI of patients with non-alcoholic fatty liver disease was significantly higher than non-alcoholic patients (P=0.003). In patients with non-alcoholic fatty liver, the

mean and standard deviation of daily smoking was 0.385±1.02 and in patients with non-alcoholic fatty liver was 0.496±1.1. There was no statistically significant difference in smoking between the two groups with and without non-alcoholic fatty liver (P <0.05). In patients with non-alcoholic fatty liver, the mean and standard deviation of vitamin E consumption per week was 0.216±1.21 and in patients with non-alcoholic fatty liver was 0.119±1.29. There was no statistically significant difference in the amount of vitamin E consumption between the two groups with and without non-alcoholic fatty liver (P <0.05) **(Table 2).**

Table 2.Comparison of body mass index, smoking, vitamin E consumption and type of oil consumed by patients with non-alcoholic and non-alcoholic fatty liver disease

P value	No affected with nonalcoholic fatty liver				Nonalcoholic fatty liver patients				Variable
	SD	Mean	Maximum	Minimum	SD	Mean	Maximum	Minimum	
0/003	3/02	24/6	44/5	19/00	4/01	29/34	44/8	20/4	**BMI**
0/680	1/1	0/696	20	0	1/02	0/385	15	0	**cigarette smoking**
0/420	1/29	0/119	4	0	1/21	0/216	7	0	**vitamin E intake**

In patients with non-alcoholic fatty liver, the highest percentage (95.01%) used other oils and in patients with non-alcoholic fatty liver, the highest percentage (74.57%) used other oils. According to Fisher's exact statistical test, a statistically significant difference was observed in the frequency distribution of the type of oil consumed by patients with non-alcoholic and non-alcoholic fatty liver (P = 0.014). Patients with non-alcoholic fatty liver used other oils more than patients with non-alcoholic fatty liver **(Table 3).**

Table 3.Comparison of the type of oil consumed by patients with non-alcoholic and non-alcoholic fatty liver disease

P value Fisher's exact test	No affected with nonalcoholic fatty liver		Nonalcoholic fatty liver patients		Type of oil consumed
0/014	Percent	Number	Percent	Number	
	11/87	7	1/6	1	**olive oil**
	13/56	8	3/3	2	**Sesame Oil**
	74/57	44	95/01	58	**Other oils**

5. Discussion: In the present study, body mass index, smoking, vitamin E consumption and type of oil consumed by patients with non-alcoholic fatty liver were compared with non-patients. Based on the findings of this study, BMI was higher than normal in both groups with and without non-alcoholic fatty liver, but was significantly higher in patients with non-alcoholic fatty liver; 29.34 vs. 24.6 (P=0.003), respectively. This finding was consistent with the findings of other studies. The results of Dehghan et al (2015) study that compared the body mass index of patients with non-alcoholic fatty liver disease with non-patients showed that the mean BMI of patients was higher than non-patients, 32.8 vs. 24.4, respectively (19).

Findings of Tayyem et al. (2019) showed that patients with non-alcoholic fatty liver disease have a higher BMI than the non-alcoholic group (20). Anderson et al (2015) also reported in a meta-analysis study that increasing BMI would significantly increase NAFLD (21). Anika Nier et al Also found in their study that BMI in children with NAFLD is higher than in non-NAFLD children (22). In a study examining the risk factors for non-alcoholic fatty liver, Moradi Kohanki et al. concluded that there was a significant relationship between BMI and NAFLD grade (23). While in some studies the chance of infection in people with body mass index was lower than the present study (24), but in most studies the increase in BMI in patients with fatty liver was significant. Obesity is therefore considered one of the most important risk factors for NAFLD (25).

The results of the present study showed that the daily smoking rate in patients with non-alcoholic and non-alcoholic fatty liver disease was 0.385 and 0.696, respectively, and there was a statistically significant difference in the average daily smoking rate of patients with non-alcoholic fatty liver disease. And there were no non-infected (P= 0.680). The findings of the present study were in the same direction as most studies and only in a small number of non-directional studies. Hyun-Suk Jung (2018) in their study that examined smoking and the risk of developing non-alcoholic fatty liver concluded that smoking is associated with an increased risk of NAFLD (26). But the results of a study by Chavez-Tapia et al (2006) on 933 patients in a teaching hospital in Mexico showed that there was no association between smoking and NAFLD (27). A cross-sectional study by Shen et al (2017) also showed no association between smoking and NAFLD (28). Therefore, smoking cannot play a major role

in the development of non-alcoholic fatty liver, although smoking has pathophysiological effects on the liver (29).

Also, the findings of the present study showed that the weekly intake of vitamin E in patients and non-patients with non-alcoholic fatty liver were 0.216 and 0.119, respectively. Mean vitamin E intake of patients with non-alcoholic fatty liver disease was not statistically significant with non-alcoholic fatty liver patients (P= 0.420). The results of the study by Nobili et al (2006) showed that taking vitamin E with vitamin C reduces ALT (30). Different studies have reported different and contradictory results on the effect of vitamin E consumption in the prevention and treatment of non-alcoholic fatty liver (12, 31, 32).

Considering that in the present study, the consumption of vitamin E in patients with and without non-alcoholic fatty liver disease was not significantly different, so the consumption of high amounts of vitamin E should be used with caution. Because there is a risk of hemorrhagic stroke and death with high doses (33) . The findings of the present study comparing the oil consumption of patients with non-alcoholic and non-alcoholic fatty liver showed that the consumption of other oils (unhealthy oils) was higher in patients with non-alcoholic fatty liver than non-patients; 95.01% vs. 74.57%, respectively, and patients with this disease used less olive and sesame oil. These findings were consistent with other studies. Various studies have shown that there is a direct link between the consumption of saturated fats and the incidence of non-alcoholic fatty liver disease (34, 35). The role of these fatty acids in increasing the risk of insulin resistance and cardiovascular disease by increasing cholesterol, triglyceride and inflammatory factor CRP(C Reactive Protein) and lowering cholesterol HDL (High Density Lipoprotein) suggests that these fatty acids may be involved. Fatty liver is involved. Some dietary sources of Tran's fatty acids include margarine, butter, and commercial frying oils (36).

Various studies have shown that in patients with non-alcoholic fatty liver disease, weight loss and adherence to a proper diet along with physical activity is one of the most appropriate treatments (37). Sesame oil can reduce the activity of the enzyme phosphatidate phosphohydrolase and thus reduce the rate of hepatic triglyceride synthesis and consequently reduce the risk of fatty liver in hypercholesterolemic diets. The study of Heydarian et al. (2013) showed a significant decrease in the mean plasma antioxidant capacity in the group with high cholesterol diet compared to the control group (38). According to the findings of the present study and other studies, it seems that the type of oil consumed has a significant effect on the development of non-alcoholic fatty liver.

6. Conclusion: In general, body mass index, healthy diet and lack of saturated fatty acids, non-smoking and consumption of antioxidants are modifiable factors in the development of non-alcoholic fatty liver that can be easily modified by lifestyle changes. Given today's lifestyle that leads to inactivity and weight gain, educational interventions to change attitudes and increase awareness of risk factors for non-alcoholic fatty liver disease seem necessary. It is recommended to use more healthy oils such as olive oil and sesame oil in the daily diet of people, and in addition to modifying the oil consumption, proper physical activity and weight loss is also recommended. Smoking as a risk factor, as well as the use of vitamin E to prevent

and treat non-alcoholic fatty liver disease, requires further studies with a larger sample size. It is recommended to take vitamin E with a doctor's prescription and supervision.

7. Study limitation: Illness of some patients who in this case tried to get information from patients Attendant. Also, one of the limitations beyond the researcher's authority was the researcher's presence to complete the questionnaire.

8. Suggestions for future studies:

- Prevalence of alcoholic fatty liver in a similar study

- Study and classification of main risk factors of non-alcoholic fatty liver

- The effect of nutrition and exercise on non-alcoholic fatty liver

- The effect of various vitamins on non-alcoholic fatty liver

Acknowledgments: The present study was approved by the Research Council of the Islamic Azad University, Khorramabad Branch in 2019 with the ethics codeIR.IAU.B.REC.1399.013. We would like to thank the Vice Chancellor for Research of the Islamic Azad University, Khorramabad Branch, and the participating patients and all those who helped us in this study.

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OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) — 8 Nov 2020

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Reviewer | **Revision** (1) — 20 Nov 2020

Dear AE,
Suggestions should be written as a paragraph.
Thanks.

REFEREE: EIC | **Revision** (1) — 24 Nov 2020

Dear Author,
Please pay attention to all comments and revise your manuscript. we are waiting for your revised manuscript.
with the regards.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision** (2) 29 Nov 2020

Dear Author,
Thank you for revising your manuscript. this manuscript in the current format is acceptable.
With the best.