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Therapeutic Effects of Vitamin E in Non-alcoholic Fatty Liver Disease: An Open-Labeled Clinical Trial

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Abstract

Non-alcoholic fatty liver disease is one of the widespread chronic liver diseases; it is ranging from simple fat buildup in the liver (steatosis) to non-alcoholic steatohepatitis with the presence of inflammation and hepatocyte injury. Vitamin E is one of the most potent antioxidants, in addition to the antioxidant effect of vitamin E; it has anti-inflammatory and anti-apoptotic properties. Lifestyle modifications are the cornerstone for non-alcoholic fatty liver management to lose weight and reduce hepatic fat content.

To assess the effects of vitamin E and lifestyle modifications on the degree of fatty infiltration in the liver, liver enzymes, and lipid profile.

This is a prospective pre-post intervention open-labeled clinical trial which was performed in Gastroenterology and Hepatology teaching hospital in Baghdad\Iraq, The duration of this study was seven months from January 2021 to July 2021, (39) Participants were included after being diagnosed with NAFLD by the specialized physician depending on ultrasonography findings, They were administered vitamin E 800IU\day for 12 weeks and advised to take low fat, low carbohydrate diet and increase physical activity. Steatosis score, liver enzymes, fasting serum glucose, and lipid profile were measured at baseline and repeated at 4 weeks and 12weeks of the study period. ANOVA test was used to compare the measures among baseline, 4 weeks, and 12 weeks of the study, least significant difference LSD was used to find out the significant measures, Pearson Chi-Square test was used to compare steatosis score throughout the study.

This study found that there is an association between steatosis score and vitamin E use with lifestyle modifications as the score reduced significantly throughout the study (P=0.0001) whereas 46.2% of the participants turned into a score (0) at 12 weeks of the study. Liver enzymes ALT, AST, and ALP did not show significant differences among baseline, 4 weeks, and 12 weeks (P=0.211, P=0.052, and P=0.352 respectively), However, AST showed significant differences between 4 weeks versus12 weeks (P=0.039) and baseline versus 12 weeks (P=0.032). LDL, VLDL, and HDL did not show significant differences among baseline, 4 weeks, and 12 weeks (P=0.569, P=0.195, and P=0.949 respectively) while total cholesterol and triglyceride showed significant difference (P=0.001and P=0.0001 respectively). BMI showed a significant difference between baseline and 12 weeks (P=0.015). Fasting serum glucose did not show a significant difference throughout the study (P=0.122).

Vitamin E with lifestyle modifications has beneficial effects for patients with NAFLD as steatosis score, total cholesterol, triglyceride, and BMI had reduced significantly during the study period.

Keywords: nonalcoholic fatty liver disease (NAFLD), steatosis score, vitamin E

التأثيرات العلاجية لفيتامينه في مرض الكبد الدهني غير الكحولي :تجربة سريرية مفتوحة ذات ذراع واحدة

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الخلاصة

مرض الكبد الدهني غير الكحولي هو أحد أمراض الكبد المزمنة المنتشرة. وهو يتراوح من تراكم الدهون البسيط في الكبد (تجمع دهني) إلى التهاب الكبد الدهني غير الكحولي مع وجود التهاب وتضرر خلايا الكبد. فيتامين هـ من أقوى مضادات الأكسدة، بالإضافة إلى أنه له تأثير مضاد للأكسدة له خصائص مضادة للالتهابات ومضادة لموت الخلايا المبرمج. تعد تعديلات نمط الحياة أهم الطرق المستخدمة في علاج الكبد الدهني غير الكحولي ولذلك لإنقاص الوزن وتقليل محتوى الدهون في الكبد.

تقييم تأثير فيتامين هـ وتعديلات نمط الحياة على درجة ارتشاح الدهون في الكبد وأنزيمات الكبد وهيئة الدهون.

هذه تجربة سريرية مرتقبة قبل وبعد التداخل ، تم إجراؤها في المستشفى التعليمي لأمراض الجهاز الهضمي والكبد في بغداد / العراق ، واستغرقت هذه الدراسة سبعة أشهر من كانون الثاني ٢٠٢١ إلى تموز ٢٠٢١. تم تضمين ٣٩ مشاركا بعد تشخيص مرض الكبد الدهني غير الكحولي لديهم من قبل الطبيب المختص اعتمادًا على نتائج الموجات فوق الصوتية ،و تم إعطاؤهم فيتامين ه ٨٠٠ وحدة

دولية يوميًا لمدة ١٢ أسبوعًا ونصحهم بتناول نظام غذائي منخفض الدهون وقليل الكربوهيدرات وزيادة النشاط البدني. تم قياس نتيجة التجمع الدهني وإنزيمات الكبد وكلوكوز مصل الدم الصائم وهيئة الدهون عند البدأ وبعد ٤ أسابيع و ١٢ أسبوعًا من فترة الدراسة.

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تم استخدام اختبار التباين ألاحادي لمقارنة متوسط المقاييس بين البدأ، و ٤ أسابيع ، و١٢ أسبوعًا من الدراسة ، وتم استخدام أختبار أقل فرق معنوي لمعرفة القراءات ذات الفروقات ألاحصائية، وتم استخدام اختبار مربع كاي لمقارنة درجة التجمع الدهني خلال فترة الدراسة.وجدت هذه الدراسة أن هناك ارتباطًا بين درجة التجمع الدهني واستخدام فيتامين هـ مع تعديلات نمط الحياة حيث انخفضت الدرجة بشكل كبير خلال الدراسة (P = ٠,٠٠٠١) حيث تحول ٢ ,٤٦ ٪ من المشاركين إلى درجة (٠) في ١٢ أسبوعًا من الدراسة. لم تظهر إنزيمات الكبد ناقلة أمين الألانين, ناقلة أمين الأسبارتات, و الفوسفاتيز القلوي فروقًا ذات دلالة إحصائية بين البداية ، ٤ أسابيع ، و ١٢ أسبوعًا (P = ٠,٢١١ ، P = ٠,٠٥٢ ، و P = ٠,٣٥٢ على التوالي) ، ومع ذلك ، أظهر ناقلة أمين الأسبارتات اختلافات كبيرة بين ٤ أسابيع مقابل ١٢ أسبوعًا (P =٠,٠٣٩) والبداية مقابل ١٢ أسبوعًا (P = ٠,٠٣٢) .لم يُظهر البروتين الدهني منخفض الكثافة, البروتين الدهني منخفض الكثافة جدا, و البروتين الدهني العالي الكثافة فروقًا ذات دلالة إحصائية بين البداية ، ٤ أسابيع ، و ١٢ أسبوعًا (P = ٠,٥٦٩ ، P = ٠,١٩٥ ، و P = ٠,٩٤٩ على التوالي) بينما أظهر الكوليسترول الكلي والدهون الثلاثية فرقًا كبيرًا (P = ٠,٠٠١ و P = ٠,٠٠٠١ على التوالي). أظهر مؤشر كتلة الجسم فرقًا كبيرًا بين البداية و ١٢ أسبوعًا (P = ٠,٠١٥) .لم يظهر كلوكوز مصل الدم أثناء الصيام فرقًا معنويًا خلال الدراسة (P = ٠,١٢٢). فيتامين (ه) مع تعديلات نمط الحياة له آثار مفيدة للمرضى الذين يعانون من مرض الكبد الدهني الغير كحولي حيث انخفضت درجة التجمع الدهني في الكبد والكوليسترول الكلي والدهون الثلاثية ومؤشر كتلة الجسم بشكل ملحوظ خلال فترة الدراسة.

الكلمات المفتاحية: مرض الكبد الدهني غير الكحولي ، درجة التجمع الدهني ، فيتامين هـ

Introduction

Non-alcoholic fatty liver disease (NAFLD) is one of the widespread chronic liver diseases, it is ranging from simple fat buildup (steatosis) to non-alcoholic steatohepatitis (NASH), which is characterized by the presence of steatosis and inflammation, as well as hepatocyte damage(1).In certain cases, NASH can develop fibrosis, which can lead to liver cirrhosis. Cirrhosis caused by NASH is the major cause of hepatocellular carcinoma and the second most common reason for liver transplantation in the United States(2).

The prevalence of NAFLD worldwide was estimated to be 25.2%, with the elevated prevalence was recorded from the Middle East and South America (31.8% and 30.4 5, respectively) while Africa recorded the lowest rates (13.5%), as had been observed in a recent meta-analysis(3).

There is a strong relationship between metabolic syndrome and nonalcoholic fatty liver disease, furthermore, NAFLD is identified as a hepatic presentation of metabolic syndrome(4). Several risk factors have been linked to NAFLD, including advanced age, obesity, insulin resistance, type 2 DM, and hyperlipidemia(5,6). Insulin resistance is a key component in the onset and progression of NAFLD. It promotes de novo lipogenesis and lipolysis leading to inflammation and change of lipid metabolism which enhances additional insulin resistance leading to excessive amounts of fatty acids in the liver which in turn causes lipotoxicity, which is the primary cause of hepatocyte impairment and pathogenicity of NAFLD(7,8).

The gold standard for diagnosing NASH and the fibrotic stage of NAFLD is liver biopsy, but it is invasive and expensive so it is not practical to be used in clinical practice(9). Several noninvasive diagnostic techniques have been used for NAFLD diagnosis which include: imaging-based and blood tests(10).

There is no single treatment for NAFLD that has been demonstrated to be completely successful, The mainstays of NAFLD management are changing dietary habits and increasing physical activity to lose weight, and reducing hepatic lipid contents as weight reduction is favorable and the degree of improvement in liver histology is proportional to the quantity of decreased weight, moreover, even without considerable weight reduction, lifestyle modifications are beneficial for NAFLD patients, particularly when patients continue the lifestyle modifications program. The majority of researches also showed that changing of lifestyle leads to reductions in risk factors for cardiovascular diseases such as serum lipid values and insulin resistance(11–13).

Vitamin E (α-tocopherol) has antioxidant, anti-inflammatory, and anti-apoptotic effects. It is considered one of the most potent chain-breaking antioxidants. There are multiple types of tocopherols and tocotrienols, including alpha, beta, and gamma tocopherols; nevertheless, the alpha-tocopherol form is the most common and active in the human body(14). It has been studied in the treatment of NASH; due to it is antioxidant property. Vitamin E at an 800 IU/day dose was found to be effective more than placebo in the PIVENS research (Pioglitazone versus vitamin E versus placebo for the treatment of non-diabetic patients with NASH); it improved liver enzymes as well as steatosis and lobular inflammation but did not affect fibrosis(15). The American Association for the Study of Liver Diseases (AASLD) and the National Institute for Health and Care Excellence (NICE) both advocate vitamin E for the management of NAFLD(16).

Objectives of the study

To assess the effects of vitamin E and lifestyle modifications on:

1. Degree of fatty infiltration in the liver.
2. Liver enzymes and lipid profile.

Materials and Methods

Study design and patient recruitment

This is a prospective open-labeled study. The participants were recruited from the Gastroenterology and Hepatology teaching hospital (tertiary center) in Baghdad. The study duration was seven months from January 2021 to July 2021. Patients were enrolled in this study after being diagnosed by a specialized physician depending on ultrasonography and after the screening of inclusion and exclusion criteria and signing of informed consent.

Inclusion criteria

1. Patients of both genders and aged between 18-65 years old.

2. Newly diagnosed with nonalcoholic fatty liver disease with any degree of fatty infiltration in the liver.

Exclusion criteria

1. Patients with a history of alcohol consumption.

2. Patients with acute liver failure and chronic liver disease.

3. Cardiac failure, renal failure, DM type 1and 2, and any severe systemic co-morbidities.

4. Previously used vitamin E or has a history of sensitivity to vitamin E.

5. Pregnant and lactating women.

6. Use of medications has drug-drug interaction with vitamin E or use drugs reported to cause fatty liver as a side effect.

7. Patients who did not complete the study.

Data collection

Patients, data were collected at baseline and after using vitamin E with lifestyle modifications at 4th weeks and 12th weeks of the study. Then measures were compared to assess the effects of vitamin E and lifestyle modifications

The following data were obtained from each patient:

1. Patient demographic information (name, age, and gender).

2. Medical history (liver disease, chronic disease, and chronic medications).

3. Patient baseline measures (weight, height, BMI, waist circumference), lab tests (fasting serum glucose, liver enzymes, lipid profile), and the degree of fatty infiltration in the liver.

All the participants were advised to take a low-fat, low carbohydrate diet, increase physical activity, vitamin E 800 IU/day was prescribed for 12 weeks, and follow up visits were at 4^{th} week and 12^{th} week of the intervention for measuring of the previous parameters.

Diagnosis and staging of NAFLD

The degree of fatty infiltration in the liver can be subjectively assessed using ultrasonography imaging. The brightness of the liver, the difference between the liver and the kidney, the US pattern of the intrahepatic vessels, liver tissue, and the diaphragm are all used to grade steatosis. Scores were graded as: normal (score 0), mild (score1), moderate (score2) and severe (score3)[17].

Statistical analysis

Frequency, percentage, mean and standard deviation were used to present the data. The comparison between baseline, 4weeks, and 12 weeks measures was performed by using of ANOVA test, and then the least significant difference (LSD) test was used to find the significant measures. Pearson Chi-square test was used to compare the categorical variables. SPSS-27 was used to analyze the data and statistical significance was evaluated when the P-value < 0.05[18].

Results

Sixty patients were enrolled in this study only 39 patients continued the study, the mean age of the participants was 46.2±11.1 years with a range of 25-65 years, and the highest percent (30.8%) was for the age group (40-49) years. Female gender was slightly higher than the male (59% and 41% respectively); the mean age of women was 50.1±11.1 with a range of (25-65) years while in men the mean was 40.2±8.6 with a range of (26-57) years. The percentage of housewives was high (43.6%) as the female gender was dominant. Hypertension was found in 12.8% of the participants had as demonstrated Table 1:

Table 1. Demographic data

		No	%
Age (years)	<30years	2	5.1
	30---39	9	23.1
	40---49	12	30.8
	50---59	9	23.1
	=>60years	7	17.9
	Mean ± SD	46.2±11.1	
	Range	25-65	
Gender	Male	16	41.0
	Female	23	59.0
	Male age: Mean ±SD	40.6±8.7	
	Range	26-57	
	Female age: Mean ±SD	50.1±11.1	
	Range	25-65	
Occupation	Governmental-employee	13	33.3
	Self-employee/Worker	9	23.1
	Housewife	17	43.6
Medical history	Hypertension	5	12.8
	No	34	87.2

Anthropometric measurements of the patients

At baseline, obese patients have the highest percent (46.2%) and this percent is still the highest to the end of the study (43.6%) while the percentage of patients with morbid obesity was reduced from (33.3%) at baseline to (12.8%) at 12weeks, the percentage of patients with normal BMI was (12.8%) at 12 weeks. There is a significant association between BMI and vitamin E use with lifestyle modifications (P=0.019) as shown in Table 2.

Table 2. BMI association with lifestyle modifications and vitamin E use at 4weeks and 12weeks of the study

BMI	Baseline		After 4wks		After 12wks		Pearson Chi-square test P-value
	No	%	No	%	No	%	
Normal (18.5-24.9)	-	-	-	-	5	12.8	**0.019***
Overweight (25-29.9)	8	20.5	13	33.3	12	30.8	
Obese (30-34.9)	18	46.2	15	38.5	17	43.6	
Morbid Obese (=>35)	13	33.3	11	28.2	5	12.8	
*Significant difference P< 0.05.							
BMI: body mass index.							

As shown in Table 3 there are no significant differences in weight and waist circumference means among baseline, 4 weeks, and 12 weeks of the study (P=0.088 and P=0.336 respectively) only BMI showed a low significant difference (P=0.049). There are significant differences in weight and BMI means between baseline and 12 weeks of the study (P=0.029 and P=0.015 respectively) while waist circumference showed no significant difference (P=0.144).

Table 3. Mean ±SD of anthropometric measurements at baseline, 4weeks, and 12weeks of the study

	Baseline	After 4wks	After 12wks	P-value			
				ANOVA test	LSD test		
					Baseline x 4wks	4wks x 12wks	Baseline x 12wks
Weight (Kg)	91.89±17.47	89.03±15.92	84.14±12.79	0.088	0.417	0.167	**0.029***
Height (cm)	165.72±10.58	165.72±10.58	165.74±10.59	-	-	-	-
BMI (Kg/m2)	33.42±5.29	32.32±4.89	30.71±4.31	**0.049***	0.317	0.145	**0.015***
Waist circumference (cm)	111.62±11.21	110.26±10.66	108.00±10.71	0.336	0.582	0.361	0.144
*Significant difference P < 0.05.							
BMI: body mass index.							

Liver enzymes and fasting serum glucose

As illustrated in Table 4 , there is no significant difference in fasting serum glucose levels among baseline, 4 weeks, and 12 weeks of the study (P= 0.122), evermore there is no significant difference between baseline and 12 weeks of the study (P=0.084).

There is no significant difference in levels of ALT, AST, and ALP among baseline, 4 weeks, and 12 weeks of the study (P=0.211, P=0.052, and P=0.352 respectively), whereas AST levels showed significant differences between 4 weeks vs. 12 weeks (P=0.039) and baseline vs.12 weeks (P=0.032) as shown in Table 4 .

Table 4. Mean ± SD of fasting serum glucose and liver enzymes at baseline, 4wks, and 12wks of the study

	Baseline	After 4wks	After 12wks	P-value			
				ANOVA test	LSD test		
					Baseline x 4wks	4wks x 12wks	Baseline x 12wks
Fasting serum glucose (mg/dL)	97.18±9.16	96.99±8.89	100.69±8.65	0.122	0.927	0.069	0.084
ALT (IU/L)	33.29±16.70	32.91±18.27	28.50±9.76	0.211	0.344	0.079	0.412
AST (IU/L)	26.38±9.99	26.23±10.43	22.08±4.70	0.052	0.938	**0.039***	**0.032***
ALP (IU/L)	94.06±31.59	93.76±31.81	86.18±14.49	0.352	0.962	0.221	0.203
*Significant difference P< 0.05 level.							
ALT: alanine aminotransferase, AST: aspartate aminotransferase, ALP: Alkaline phosphatase							

Lipid profile

There are no significant differences in levels of LDL, VLDL, and HDL among baseline, 4 weeks, and 12 weeks of the study (P=0.569, P=0.195, and P= 0.949 respectively) while levels of total cholesterol and triglyceride showed significant differences (P=0.001 and P=0.0001 respectively), Furthermore total cholesterol levels showed a significant difference between baseline vs. 4 weeks (P=0.042) and baseline vs. 12 weeks (P=0.0001) whereas levels of triglyceride showed a significant difference between baseline vs. 4 weeks (P=0.009), 4 weeks vs. 12 weeks (P=0.023), and baseline vs.12 weeks (P=0.0001) as showed in Table 5:

Table 5. Mean ±SD of Lipid profile at baseline, after 4wks and 12wks of the study

Lipid profile	Baseline	After 4wks	After 12wks	p-value			
				ANOVA test	LSD test		
					Baseline x 4wks	4wks x 12wks	Baseline x 12wks
LDL (mg/dL)	113.21±40.61	104.90±33.94	111.50±34.30	0.569	0.389	0.371	0.974
VLDL (mg/dL)	32.01±11.26	28.44±6.49	29.98±7.61	0.195	0.072	0.437	0.303
HDL (mg/dL)	42.19±9.96	42.43±9.68	42.85±7.24	0.949	0.908	0.838	0.750
Total Cholesterol (mg/dL)	182.53±43.56	167.42±25.80	154.87±24.46	**0.001***	**0.042***	0.091	**0.0001***
Triglycerides (mg/dL)	166.08±54.59	141.29±33.38	119.98±30.48	**0.0001***	**0.009***	**0.023***	**0.0001***
*Significant difference P< 0.05 level.							
LDL: low-density lipoprotein, VLDL: very low-density lipoprotein, HDL: high-density lipoprotein							

Steatosis score

Steatosis score was represented as mild, moderate, and severe depending on ultrasonography findings, the highest percentage of patients have mild steatosis (59%) where moderate steatosis and severe steatosis were (33.3% and 7.7% respectively), the percentage of patients who have score 0 (normal liver echogenicity) is (46.2%) at 12weeks. There is a significant association between steatosis score and vitamin E use with lifestyle modifications (p=0.0001) as demonstrated in Table 6.

Table 6. Steatosis score at baseline, 4wks, and 12wks of the study

Steatosis score	Baseline		After 4wks		After 12wks		Pearson Chi-square test P-value
	No	%	No	%	No	%	
Normal (0)	-	-	3	7.7	18	46.2	**0.0001***
Mild (1)	23	59.0	21	53.8	15	38.5	
Moderate (2)	13	33.3	13	33.3	4	10.3	
Severe (3)	3	7.7	2	5.1	2	5.1	
*Significant difference P< 0.05 level.							

Discussion

Non-alcoholic fatty liver disease represents the buildup of excess fats in the liver, as observed by imaging or histology in the absence of any secondary etiology and considerable alcohol intake. Worldwide urbanization and modernization in the twentieth and twenty-first centuries have been connected to undesirable lifestyle patterns. As a result, the mean worldwide body mass index and occurrence of obesity, which are the main causes of NAFLD, have increased markedly during the previous three decades. NAFLD is now the most widespread chronic liver disease in developed countries[11,13,19].

In this study the percentage of female patients was slightly higher than male patients. Interestingly, the gender-specific predominance of NAFLD is associated with age: the prevalence of NAFLD in men rises from youth to middle age, whereas in women it rises approximately 10 years later after men and increases after the age of 50 years[20]. However, certain studies revealed that the prevalence in men was higher than in women while others showed vice versa[8].

Concerning the correlation of the type of occupation with NAFLD, a cross-sectional study had revealed that working for prolonged time are linked to a greater likelihood of NAFLD than shorter or standard working times as working for a long time is associated with unhealthy lifestyle such as eating fast food, decreasing of physical activity, and reduction of sleeping hours[21]. A cross-sectional study from China found that the prevalence of NAFLD was higher in women than in men as women were mostly housewives with little physical activity[22], however, this study showed that the percentage of housewives was the highest followed by governmental-employee and self-employed.

In this study fasting serum glucose did not change significantly during the study period, even though its mean was increased at 12 weeks of the study but remained within the normal range, however, in a prospective cohort study oral glucose tolerance test was used to detect hyperglycemia in NAFLD patients, the study showed that older age, elevated BMI, and low HDL levels all of which anticipated the existence of the hyperglycemia, the study recommends the use of oral glucose tolerance test to screen patients with NAFLD who had one or more of the aforementioned factors to detect and treat impaired glucose metabolism effectively[23]. In this study 12.8% of the participants had hypertension, clinical and experimental findings show that NAFLD may anticipate and/or increase the development of diabetes, hypertension, and cardiovascular disease and the risk of these disorders appears to be linked to NAFLD severity, as patients with NASH and hepatic fibrosis have a higher risk than those with simple steatosis to develop hypertension, type 2 diabetes, and cardiovascular disease[24].

The mean weight, BMI, and waist girth was reduced during this study, at 12wks 12.8% of patients were had normal BMI, weight loss has positive effects on NAFLD patients as exhibited by many studies which demonstrated that weight loss of 5-7% is primarily linked to a reduction in hepatic steatosis, weight loss of 7-10 % increase probability of NASH resolution and fibrosis regression while weight reduction ≥ 10% linked to highest chances of NASH cure and fibrosis reversion[25,26]. According to American and European guidelines, the primary clinical suggestion for the treatment of NAFLD is lifestyle modifications to obtain progressive weight loss, rising of physical activity, and changing of dietary habits, the type of exercise should be customized according to the decisions of the patients to be sustained over time[27,28].

This study showed that the levels of liver enzymes did not change significantly among baseline, 4 weeks, and 12 weeks of the study period since many of the participants had normal liver enzymes at baseline, normal ALT levels in NAFLD\NASH patients may be related to genetic causes and personal variations, however, patients with normal ALT levels had similar histological and clinical characteristics to patients with high ALT levels[29]. Only levels of AST showed significant difference throughout the study because AST levels were normal in all the participants at 12 weeks. However, recent reviews showed that ALT values were within normal ranges in approximately 80% of patients with NAFLD, and aminotransferase values did not correspond to the extent of liver fibrosis so increased ALT serum levels do not reliably determine disease severity[30,31], whereas a recent systematic review and meta-analysis revealed that 25% of NAFLD patients and 19% of NASH patients had normal ALT levels so the ALT value as an important metabolic marker does not have enough precision to accurately diagnose NAFLD and NASH, furthermore all protocols agree that normal liver enzyme values may not rule out NAFLD[29,32].

Dyslipidemia is common in patients with NAFLD and it is attributed to insulin resistance in liver and adipose tissue. In addition, The production of VLDL is enhanced to compensate for triglyceride buildup in the liver, and the expression of LDL receptors is reduced, resulting in higher amounts of VLDL and LDL in the blood[33–35], In this study, many participants had an abnormal lipid profile at baseline especially triglyceride levels, at 12 weeks, levels of total cholesterol and triglyceride showed significant changes while levels of LDL, VLDL, and HDL did not. This is because the levels of LDL and VLDL remain elevated in some patients who still had steatosis, moreover, LDL and VLDL levels were slightly elevated in some participants who had scored (0) at 12 weeks of the study whereas HDL levels were normal in many participants at baseline and remain low in some participants who still had steatosis at the end of the study. However, a longitudinal study from Korea found that patients with NAFLD were less likely to attain their LDL cholesterol goals than those without the disease, even though the predicted percentage of patients who did not reach their LDL cholesterol targets varied over time, it was generally greater in the NAFLD group than in the normal group[36], furthermore, a retrospective study included 431 patients, revealed that higher cholesterol and triglyceride concentrations, as well as lower HDL concentrations, were presented in more than half of the patients and 81.81% of patients with grade 3 liver steatosis had low HDL levels, which indicates that a greater grade of steatosis raises the risk of hyperlipidemia[37], the results of these studies may explain the reasons of high LDL levels in some patients at the end of the study, and normal levels of HDL at baseline as 59% of participants had mild steatosis while the percentage of participants with severe steatosis was 7.

There was an improvement in steatosis score because 46.2% of the study participants had scored (0) at the end of the study and this is consistent with previous studies which found that ALT, AST, histological alterations, steatosis, inflammation, and hepatocellular ballooning are largely reduced by vitamin E[38], which is known as a chain-breaking antioxidant because of its capacity to inhibit the progression of lipid peroxidation since the development of fatty liver disorders has been linked to oxidative stress and lipid peroxidation[39,40]. Besides the antioxidant properties of vitamin E, α-tocopherol levels in plasma are shown to be lower in NAFLD\NASH patients in comparison with healthy controls[41,42]. Furthermore, a recent systematic review and meta-analysis demonstrated that vitamin E improves both hepatic enzymes and histological markers and these results are independent of BMI therefore patients with NAFLD who are unable to adhere to lifestyle changes may benefit from vitamin E treatment as a second option[43], as the rates of debility and quit are high reaching 40% and 50% respectively during lifestyle intervention regimens, even though lifestyle alterations are considered as first-line treatment for NAFLD[16].

Limitations of this study: it is a single-center study, absence of control group, short time of the study since each participant need follow up for 3 months, small sample size due to loss of the participants during the study and this mainly belong to COVID 19 pandemic also this disease is silent so the patients feel they are well and do not need to continue the treatment.

Conclusions and recommendations

This study had shown that vitamin E with changing of lifestyle has beneficial effects on patients with NAFLD since steatosis score, total cholesterol, triglyceride, and BMI had been reduced significantly through the study period. Further studies are required with a larger sample size and a longer study period since some patients need more than 3 months to achieve a response to vitamin E.

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