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MEDITERRANEAN-STYLE DIET FOR NONALCOHOLIC FATTY LIVER DISEASE. LITERATURE REVIEW

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Abstract

Introduction. Nonalcoholic fatty liver disease (NAFLD) is a common disease associated with metabolic syndrome and characterised by fat accumulation in hepatocytes. The prevalence of NAFLD in adults is estimated to be 25%–30% in the general population.

This review **aimed** to investigate the effect of the Mediterranean diet on non-alcoholic fatty liver disease and its metabolic complications.

Search Strategy: English-written articles in peer-reviewed journals were identified by searching PubMed from 2017 to 2024. The search strategy combined words from the following concepts: Mediterranean diet, metabolic syndrome, non-alcoholic fatty liver disease, lipid profile, and liver function. *Inclusion criteria:* Evidence level A, B publications: meta-analyses, systematic reviews, cohort and cross-sectional studies. *Exclusion criteria:* expert opinion in the form of short communications, promotional articles.

The results show that the Mediterranean diet has a positive effect on the lipid profile, helps in the regression of liver fibrosis and inflammation, and improves metabolic parameters such as insulin resistance. Moreover, the reported beneficial effects (antioxidant, anti-inflammatory) of Mediterranean-style diets provide high levels of phytochemicals, including dietary polyphenols.

Conclusions. The Mediterranean diet should be recommended for patients with nonalcoholic fatty liver disease. In case of updating the Kazakhstani clinical protocol for nonalcoholic fatty liver disease. The Mediterranean diet should be involved as a Public Health measure.

Key words: *Mediterranean diet, metabolic syndrome, non-alcoholic fatty liver disease, lipid profile, liver function.*

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Резюме

СРЕДИЗЕМНОМОРСКАЯ ДИЕТА ПРИ НЕАЛКОГОЛЬНОЙ ЖИРОВОЙ БОЛЕЗНИ ПЕЧЕНИ. ОБЗОР ЛИТЕРАТУРЫ

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Актуальность. Неалкогольная жировая болезнь печени - распространенное заболевание, связанное с метаболическим синдромом и характеризующееся накоплением жира в гепатоцитах. Распространенность НАЖБП среди взрослых оценивается в 25–30% в общей популяции.

Цель данного обзора — изучить влияние Средиземноморской диеты на течение неалкогольной жировой болезни печени и её метаболические осложнения.

Стратегия поиска: Статьи в рецензируемых журналах на английском языке были найдены в PubMed с 2017 по 2024 год. Стратегия поиска включала следующие ключевые слова: средиземноморская диета, метаболический синдром, неалкогольная жировая болезнь печени, липидный профиль, функция печени. *Критерии включения:* публикации уровня доказательности А, В: метаанализы, систематические обзоры, когортные и поперечные исследования. *Критерии исключения:* экспертное мнение в форме кратких сообщений, рекламных статей.

Результаты исследования. Результаты показывают, что средиземноморская диета оказывает положительное влияние на липидный профиль, помогает в регрессии фиброза печени и воспаления и улучшает метаболические параметры, такие как резистентность к инсулину. Более того, средиземноморские диеты обеспечивают высокий уровень фитохимических веществ, включая диетические полифенолы, которые, как сообщается, оказывают полезные эффекты, включая антиоксидантные, противовоспалительные.

Выводы. Средиземноморскую диету следует рекомендовать пациентам с неалкогольной жировой болезнью печени. В случае обновления казахстанского клинического протокола по неалкогольной жировой болезни печени средиземноморская диета должна быть включена в качестве меры общественного здравоохранения.

Ключевые слова: средиземноморская диета, метаболический синдром, неалкогольная жировая болезнь печени, липидный профиль, функция печени.

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Түйіндеме

БАУЫРДЫҢ АЛКОГОЛЬДЫ ЕМЕС МАЙЛЫ АУРУЫ ЖЕРОРТА ТЕҢІЗДІК ДИЕТА. ӘДЕБИЕТТІК ШОЛУ

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Кіріспе. Алкогольсіз майлы бауыр ауруы - метаболикалық синдроммен байланысты және гепатоциттерде майдың жиналуымен сипатталатын кең таралған ауру. Ересектердегі NAFLD таралуы жалпы популяцияда 25% -30% құрайды.

Бұл шолудың мақсаты - жерорта теңізі диетасының алкогольсіз майлы бауыр ауруы және оның метаболикалық асқынуларының ағымына әсерін зерттеу болып табылады.

Іздеу стратегиясы:

Рецензияланған журналдардағы ағылшын тілінде жазылған мақалалар 2017-2024 жылдар аралығында PubMed дерекқорын іздеу арқылы анықталды. Іздеу стратегиясы келесі ұғымдардағы сөздерді біріктіруді қамтыды: Жерорта теңізі диетасы, метаболикалық синдром, алкогольсіз майлы бауыр ауруы, липидті профиль, бауыр функциясы. *Қосылу критерийлері:* Дәлелдер деңгейі А, В жарияланымдары: мета-талдаулар, жүйелі шолулар, когорттық және қималық зерттеулер. *Алып тастау критерийлері:* қысқаша хабарламалар, жарнамалық мақалалар түріндегі сараптамалық қорытынды.

Нәтиже. Жерорта теңізі диетасының липидті профильге оң әсер ететінін, бауыр фиброзының және қабынуының регрессиясына көмектесетінін және инсулинге төзімділік сияқты метаболикалық параметрлерді жақсартатынын көрсетеді. Сонымен қатар, жерорта теңізі үлгісіндегі диеталар антиоксидантты, қабынуға қарсы, пайдалы әсерлері туралы хабарланған диеталық полифенолдарды қоса, фитохимиялық заттардың жоғары деңгейін қамтамасыз етеді.

Қорытынды. Алкогольсіз майлы бауыр ауруы бар науқастарға Жерорта теңізі диетасы ұсынылуы керек. Алкогольсіз майлы бауыр ауруы бойынша қазақстандық клиникалық хаттаманы жаңарту жағдайында Қоғамдық денсаулық сақтау шарасы ретінде Жерорта теңізі диетасын қосу қажет.

Түйінді сөздер: Жерорта теңізі диетасы, метаболикалық синдром, алкогольсіз май бауыр ауруы, липидті профиль, бауыр қызметі.

Дәйексөз үшін: Рахметова В.С., Саркулова С.М., Дербисалина Г.А., Бедельбаева Г.Г., Амирханова Л.М., Смаилова Д.С. Бауырдың алкогольды емес майлы ауруы жерорта теңіздік диета. Әдебиеттік шолу // Ғылым және Денсаулық сақтау. 2025. Vol.27 (3), Б. 267-274. doi 10.34689/SH.2025.27.3.028

Introduction

Nonalcoholic fatty liver disease (NAFLD) is characterized by triacylglyceride accumulation in hepatocytes [32], it encompasses different abnormalities, ranging from a simple increase in intrahepatic lipid content (steatosis, nonalcoholic fatty liver, NAFL) to nonalcoholic steatohepatitis (NASH) with various degrees of necrotic inflammation, fibrosis, and ultimately, cirrhosis [29].

Males are more likely than females to have NAFLD, with an estimated 47 cases per 1,000 people worldwide [57]. Metabolic liver damage affects approximately 25% of the world population [24], among whom the proportion of liver disease caused by NAFLD was 45.8% [22]. Insulin resistance is a recognized mechanism that leads to fatty liver disease development [50]. Impairment of glucose and lipid metabolic pathways is most likely behind the increase in people with NAFLD [55], mainly due to obesity and diabetes [44].

Histopathological analysis remains the 'gold standard' to diagnose liver injury. However, invasiveness, risk, and cost are issues [3]. Moreover, NAFLD brings a heavy economic burden, increasing demand for liver transplantation in patients with liver cirrhosis and end-stage liver disease [69]. Severe liver fibrosis requires aggressive clinical management and efforts to reduce underlying obesity. For instance, it is centered on lifestyle, medications, surgical or endoscopic interventions, and

metabolic derangements like prediabetes, type 2 diabetes, hypertension, hyperlipidemia, and others [9].


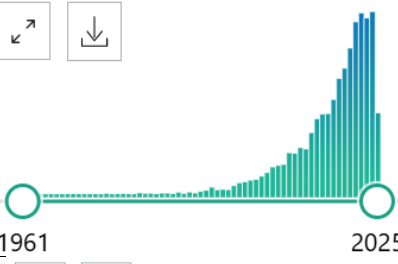
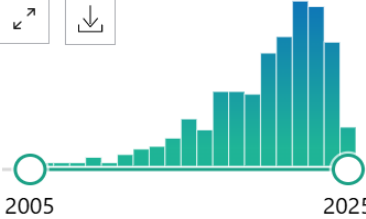
The most plausible factors contributing to NAFLD are genetic, epigenetic, and environmental [65]. Age, gender, ethnicity, and duration of fatty liver disease are epigenetic factors. Dietary habits, physical activity, and socioeconomic factors are environmental factors [12] that influence the development of metabolic syndrome [25]. Nowadays, the Mediterranean diet is recommended by researchers, which has been proven to affect the regression of inflammation and liver fibrosis [61] [14] due to the anti-inflammatory effects of the foods [54]. Despite short-term observation periods in studies, the Mediterranean diet shows potential to improve hepatic function and metabolic disorders in patients with NAFLD. Caloric restriction plays a pivotal role in weight loss and liver fat reduction, and the traditional reduced-calorie diet has a comparable effect to the Mediterranean diet [20].

Objective. This review aimed to investigate the effect of the Mediterranean diet on non-alcoholic fatty liver disease and its metabolic complications.

Search Strategy. English-written articles were identified by searching PubMed from 2017 to 2024 (Table 1). The search strategy combined words from the following concepts: Mediterranean diet, metabolic syndrome, non-alcoholic fatty liver disease, lipid profile, liver function.

Table 1.

Search way in PubMed (included 60 articles).

Kew words	Publication date 2017-2025	Text availability – free full-text	Publications related to the given keywords by years
Nonalcoholic fatty liver disease	32,954 results	20,812 results	
Mediterranean diet	8,466 results	5,952 results	
Nonalcoholic fatty liver disease and Mediterranean diet	303 results	223 results	

Inclusion criteria: Evidence level A, B publications: meta-analyses, systematic reviews, cohort and cross-sectional studies.

Exclusion criteria: expert opinion in the form of short communications, promotional articles.

Research Results.

Public Health Policy for NAFLD and the Mediterranean diet

With the increasing prevalence of obesity and type 2 diabetes mellitus and an aging population, the prevalence of NAFLD is increasing worldwide [64]. That is why NAFLD is becoming a growing challenge for public health [47].

Moreover, it is currently the fastest-growing indication for liver transplantation [10]. NAFLD causes ongoing medical expenses, financial losses, and a decline in the quality of life [48]. High-quality diets, physical activity, and socioeconomic status were associated with a lower risk of NAFLD [63].

NAFLD has received little attention from the global public health community. There is only a nascent global public health

movement addressing NAFLD [30]. According to the global NAFLD policy review and preparedness index for 102 countries (Fig.1), no country has a national or sub-national strategy for NAFLD, about a third of countries ($n = 32/102$) are ready to address this silent public health challenge (preparedness index), only 32 countries had national NAFLD clinical guidelines; A comprehensive NAFLD public health response is lacking in all 102 countries [31].

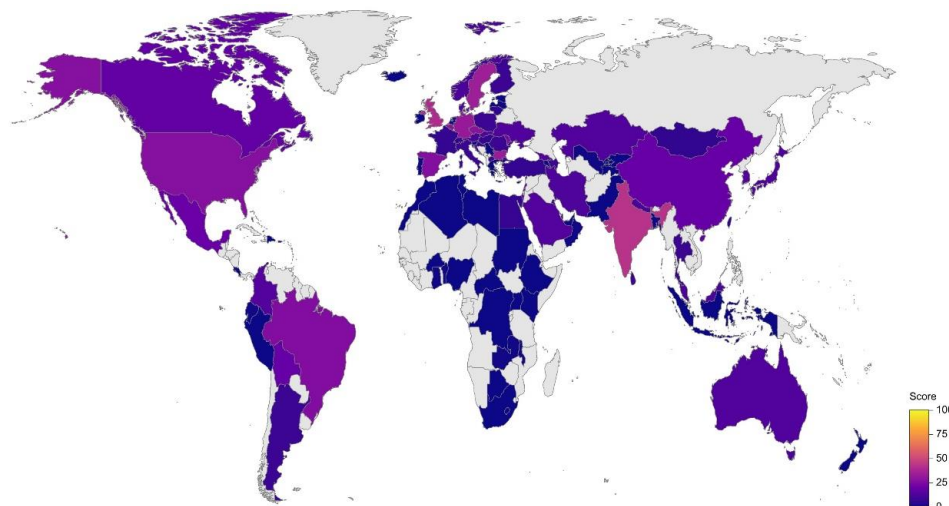


Figure 1. NAFLD preparedness index scores for 102 countries [31].

In Table 2 current situation of NAFLD in Kazakhstan is shown for further steps in making decisions in the Public Health field.

It is important to follow strategies to improve adherence:

1. Web-based approach – a comprehensive, structured web-based program leads to increasing awareness.
2. Awareness – Mass media information is known to be associated with greater adoption of the Mediterranean lifestyle.
3. Public Health Policy – Environmental risk factors are modifiable; implementing public health policies can tackle a sedentary lifestyle and bad eating habits from early childhood [23].

Mediterranean diet

Since Ancel Keys established the Mediterranean diet in the 1960s [28], numerous epidemiological studies have examined the relationship between the Mediterranean diet and health

[53]. Over the last few decades, MedStyle has been promoted worldwide as the healthiest dietary [37], adhering to the so-called food pyramid [43] with the following daily dietary intake: vegetables: 3–9 servings, fruits: 0.5–2 servings, cereals: 1–13 servings, olive oil: up to 8 servings [8]. Vegetables and fruits contain many nutrients, including vitamins A, C, K, E, B6, folic acid, copper, magnesium, iron, thiamine, niacin, and choline [70]. The low consumption of red meat and sweets and moderate consumption of wine at meals are included in the Mediterranean diet [7]. That is why the Mediterranean diet can be considered an easy-to-implement and safe lifestyle intervention to promote proper sleep hygiene [52].

The Med Diet 4.0 framework was developed between 2014 and 2015, assessed by following potential indicators of the sustainability of the Mediterranean diet: A. Nutrition and health, B. Environment, C. Economy, D. Society and culture [18].

Table 2.

Public Health Policy for NAFLD in Kazakhstan.

Public Health Issues	Current situation
National or sub-national strategy for NAFLD in Kazakhstan	No
Disease management program for NAFLD in Kazakhstan	No
Clinical Guideline for NAFLD	Yes (2015) should be updated as soon as possible
Does Mediterranean diet recommend in Clinical Guideline for NAFLD	No
Screening program	No

Mediterranean diet for NAFLD. According to a systematic review, the Mediterranean diet reduced liver stiffness and significantly reduced total cholesterol [1] [26]. However, the Mediterranean diet may reduce indirect and direct outcomes related to the severity of NAFLD, like liver fibrosis, total cholesterol, and body mass index [15].

In a prospective randomized study conducted in Spain among 155 patients aged 40–60 years with a BMI between 27–40 kg/m², the effect of personalized nutrition based on the Mediterranean diet for 6–12 months was evaluated. The

subjects were divided into 3 control groups in a 1:1:1 ratio: using a traditional diet with reduced calories, a Mediterranean diet, and a Mediterranean diet with physical activity. In all three intervention groups, after 6 months, some improvements were registered: BMI decreased, ALT, insulin levels, Hb1Ac, diastolic blood pressure and HDL cholesterol levels [45]. The reduced total caloric intake leads to the reduction of transaminase levels and insulin resistance in patients with obesity and fatty liver disease, regardless of the composition of the diet (low-carbohydrate, lean or balanced) [40].

In a randomized controlled trial registered in Australia-New Zealand involving 42 participants who were divided into 2 groups: using a traditional hypocaloric diet and a Mediterranean diet. As a result of the study, the group using the traditional hypocaloric diet showed a significant decrease in liver enzymes compared to the control group that used the Mediterranean diet [4] [35]. The weight reduction in the first group almost reached 5% (from 89.8 ± 24.5 kg to 85.8 ± 18.14 kg); whereas the group using the Mediterranean diet added 1.6 kg (from 87.7 ± 21.1 to 89.3 ± 22.8). The amount of visceral fat was significantly reduced in both groups [41]. The results of this randomized clinical trial showed that the Mediterranean diet had no significant effect on hepatic steatosis and did not outperform a traditional hypocaloric diet in an Australian cohort of patients with NAFLD [21].

A study conducted in Spain 2019 evaluated the effects of two personalised calorie-restricted dietary strategies differing in several dietary factors (macronutrients, fibre, meal frequency, total antioxidant capacity and adherence to the Mediterranean diet) on liver health and biochemical markers in patients with NAFLD after a 6-month follow-up. Both groups achieved comparable outcomes on the

assessed measures, including weight loss as well as reductions in liver fat and liver volume. There were no significant differences in changes between the intervention groups [31].

Higher adherence to the Mediterranean diet correlated with a lower prevalence of hepatic steatosis. This suggests that adhering to the Mediterranean diet may reduce the risk of fatty liver disease [27].

According to the American and European associations for the study of the liver, Diet, weight loss, and physical activity are the cornerstone of every treatment for NAFLD [46]. A healthy diet and regular exercise could help people lose weight and control the progression of NAFLD [8]. Mediterranean diet can reduce liver fat even without weight loss and is the most recommended dietary pattern for NAFLD [49]. In recent years, a growing body of evidence has supported the idea that the Mediterranean diet could be a nutritional profile for the prevention and treatment of NAFLD patients [5].

In Table 3, we tried to highlight the main Health Benefits Mediterranean diet for patients with Nonalcoholic fatty liver disease based on studies.

Table 3.

Benefits of the Mediterranean diet for patients with Nonalcoholic fatty liver disease based on studies.

Health Benefits	Study design of research/Sample Size	Evidence-based information
Weight loss	88 Chinese females with NAFLD	Mild weight loss caused by a Mediterranean-style diet modified for Asians has numerous health benefits in females with NAFLD. Supplementing with pentadecanoic acid (C15:0) decreases LDL cholesterol and may promote positive alterations in the gut microbiota [17].
Reducing total cholesterol	Ten randomized controlled trials	The review of RCTs confirmed the great potential of the Mediterranean diet on NAFLD severity due to a significant reduction in total cholesterol and liver stiffness [12].
Antioxidant effect	Review	Numerous studies have shown that polyphenols are the most abundant antioxidants in the Mediterranean diet [42].
Anti-inflammatory effect	Review	The increased intake of vegetables, whole grains, legumes, fish, fruits, and olive oil is included in the Mediterranean diet and the Dietary Approaches to Stop Hypertension (DASH) diet, which have anti-inflammatory effects [2].

The Mediterranean diet is a good choice for NAFLD treatment. Still, the evidence behind this recommendation is very low because lots of differences exist in the inclusion/exclusion criteria for a few patients [60] with comorbid conditions. NAFLD is associated with several comorbidities, which is still under investigation [33]. For instance, a growing number of studies indicate

that NAFLD is strongly associated with an increased risk of major CVD events and other cardiac complications [56]. NAFLD increases the risk of incident chronic kidney disease [34], colon cancer, and precancerous lesions as well [67].

In Table 4, we demonstrated the efficiency of various types of diet for NAFLD.

Table 4

Efficiency of varies types of diet for NAFLD.

Diet types	Food list	Recommend Yes/No
1	2	3
Mediterranean diet	The Mediterranean diet is characterized by a high percentage of fruits, vegetables, legumes, grains, white meat, and fish, with olive oil serving as the primary source of fat. At least 35% of the calories in this diet come from fats, 15% from proteins, and no more than 50% from carbohydrates [59].	Yes The Mediterranean diet is a safe and effective method for treating overweight, visceral obesity, and serum transaminase in patients with NAFLD, therefore establishing that it should be the first step in a treatment program for patient with NAFLD [13].
Western diet	This diet includes an abundance of refined and processed meals, red meat, processed meat, sugary drinks, snacks, cakes, biscuits, eggs, and butter. It includes excessive calorie consumption, saturated fats, animal protein, sugar, cholesterol, and salt[11].	No The Western diet is associated with weight gain, obesity, and, more recently, NAFLD [39]. Importantly, NAFLD-related liver failure is one of the major causes of liver transplantation in the Western world [6].

Continuation of Table 4.

1	2	3
Vegan diet	plant-based foods like fruit, vegetables, grains, legumes/beans, nuts and seeds [36].	There is no evidence on the possible benefit of vegan diets in NAFLD and/or nonalcoholic steatohepatitis (NASH) [16].
Ketogenic diet	The ketogenic diet is based on relatively low dietary carbs, with varied proportions of protein and fat. The standard ketogenic diet consists of one gram of protein per kilogram of body weight, 10-15 grams of carbohydrates per day, with the remainder of calories coming from fat. The purpose of the diet is to cause ketosis [38]. The findings imply that ketosis may exert positive benefits independent of dietary content, and so necessitates studies aimed at determining the particular function played by ketone bodies in NAFLD pathogenesis, perhaps paving the way for new treatment targets and techniques [66].	There is a shortage of well-designed studies in this area, so investigation of this scientific topic should be a priority of research in the next years. [19].
DASH diet	Grains, low-fat dairy products, yogurt, olive oil, and chocolate [58]	Adherence to the DASH diet may be effective in managing the NAFLD [51]. It is proven that the DASH diet has a lower association with non-alcoholic fatty liver disease in middle-aged and elderly adults [68]
Low-fat diet	A general rule is that if a food provides 100 calories and 3 grams or less of fat, it is a low-fat food. Common examples include vegetables, fruits, whole grain cereals, egg whites, chicken and turkey breast without skin, beans, lentils, peas, seafood, and low-fat dairy, among others [12].	All calorie-restricted dietary therapies are effective in lowering weight, liver fat content, and liver enzymes in people with NAFLD. Low-fat diets appear to be particularly effective in lowering transaminase levels. Additional research is required to investigate diet intensity, duration, and long-term outcomes [62].

Conclusion.

The Mediterranean diet should be recommended for patients with nonalcoholic fatty liver disease. In case of updating the Kazakhstani clinical protocol for nonalcoholic fatty liver disease. A Mediterranean diet should be involved as a Public Health measure.

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Authors' contributions:

Venera S. Rakhmetova - Guiding the process of writing a manuscript, quality assessment;

Saule M. Sarkulova - Searching articles, quality assessment;

Gulmira A. Derbissalina - Editing the manuscript;

Gulnar G. Bedelbaeva - Contributions to conceptualisation and methodology;

Liana M. Amirkhanova - Searching articles;

Diriga S. Smailova - Editing the manuscript, final corrections.

The final manuscript was approved by all the authors.

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