



Vitamin D Supplementation Increases the Aerobic Training Effects on Anthropometric Indices in Elderly Women with Non-Alcoholic Fatty Liver Disease and Vitamin D Deficiency

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Received 2019 April 21; Revised 2019 June 23; Accepted 2019 June 24.

Abstract

Background: Recent studies indicate that aerobic training may affect non-alcoholic fatty liver disease (NAFLD). Besides, vitamin D and NAFLD are known to have more than just an association.

Objectives: This study aimed to examine the effects of vitamin D supplementation, combined with aerobic training, on anthropometric indices in elderly women with NAFLD and vitamin D deficiency.

Methods: We randomly divided 40 elderly women with NAFLD and vitamin D deficiency into four groups: aerobic training + vitamin D supplementation (AT + Vit. D), aerobic training (AT), vitamin D supplementation (Vit. D), and control (C). The AT protocol consisted of 40 - 60 minutes of aerobic training at 60% - 75% of HR_{max} three times a week for eight weeks. The anthropometric indices included body weight (BW), body mass index (BMI), body fat percentage (BFP), and waist-hip ratio (WHR) measured at the start and after eight weeks of the study. Data were analyzed by paired *t*-test and ANOVA using SPSS version 21.0 software at a significance level of *P* < 0.05.

Results: Anthropometric indices (BW, BMI, BFP, and WHR) significantly changed in all groups, with a significant increment in the control group and decrement in the AT + Vit. D, AT, and Vit. D groups. No significant differences were observed between the AT + Vit. D, AT, and Vit. D groups in the measured variables.

Conclusions: Vitamin D supplementation combined with aerobic training improves the anthropometric indices in elderly women with NAFLD.

Keywords: Exercise, Vitamin D Deficiency, Anthropometric Indices, Non-Alcoholic Fatty Liver Disease

1. Background

Non-alcoholic fatty liver disease (NAFLD) is a type of common, chronic, and progressive fatty liver disease (1). It is similar to alcoholic fatty liver disease, with the exception that there is no alcohol abuse (2). The prevalence of NAFLD is reported between 3% and 25% in the general populations of different countries (3), 20% to 30% in developing countries (4), and more than 34% in adults in the United States (5). Although the exact causes of NAFLD are still unknown, the results of available studies indicate that there is a strong association between NAFLD and sedentary lifestyle, inappropriate nutrition, obesity, type 2 diabetes, and increased free fatty acids that may increase excess fat building up in the liver, resulting in new liver lipogenesis and beta-oxidation disorders (3, 6). In addition, increasing age causes both structural and functional undesirable alterations in the liver (7). As the liver volume decreases, the

first phase of drug metabolism drops off gradually in the liver, the expression of various types of proteins alters, and hepatobiliary function decreases (8). In women, in addition to the mentioned causes, the menopause period leads to adverse changes in body composition and lipid distribution, which increases the risk of coronary artery disease (CAD) and NAFLD (9).

Nowadays, weight loss is recognized as the only definitive treatment for NAFLD and lifestyle intervention is the only part of its management. Physical activity and diet can potentially contribute to weight loss and subsequently, liver fat reduction although it is difficult to achieve and maintain the optimal weight (10). After 16 weeks of treadmill training, Kawanishi et al. reported increased liver fat and plasma alanine aminotransferase (ALT) activity in rats with NAFLD consuming a high-fat/high-sugar diet, while the control group showed liver damage (11). Another study showed that eight weeks of aerobic training and regular

endurance training were effective in NAFLD (12). However, there are some conflicting results. Devries et al. noted that 12-week endurance training did not have a significant effect on liver fat and ALT concentration; in addition, endurance training had no positive effect on liver fat and enzymes in obese people (13).

Vitamin D deficiency has recently been reported in many countries (14, 15). Its prevalence in Iran is 47.85% in women and 34.75% in men (16, 17). The higher prevalence of vitamin D deficiency is associated with a greater prevalence of obesity in the world (18, 19). Recent epidemiological studies also show that low levels of serum vitamin D are associated with NAFLD (20). Vitamin D deficiency impairs the function of various cells, including the endocrine system and pancreas, by altering the metabolites function (21). Therefore, vitamin D supplementation can be effective in reducing vitamin D deficiency and its associated complications, especially in countries such as Iran with no implemented vitamin D fortification program. A national health and nutrition assessment on 1287 adult participants disclosed that patients with NAFLD and elevated levels of ALT had decreased levels of 25 hydroxyvitamin D (25-OHD) (22). The results of some cross-sectional studies indicate an inverse relationship between 25-OHD levels and anthropometric indices (23, 24). Rocha et al. evaluated the association of undesirable anthropometric indices in 81 patients with NAFLD and reported that body mass index and waist circumferences were highly associated with insulin resistance and metabolic syndrome (25). Moreover, it is known that waist circumference WC and dorsocervical lipohypertrophy (DCL) are the predictors of metabolic risk profile and NAFLD and they are strongly associated with the severity of steatohepatitis. In addition, WC and BMI doubled the contribution of DCL to the severity of nonalcoholic steatohepatitis (26). Limited clinical trials have studied the interaction effect of aerobic training and vitamin D supplementation while it is important to improve anthropometric indices, liver enzymes and glycemic indexes in NAFLD.

2. Objectives

We aimed to evaluate the interaction effect of aerobic training and vitamin D on anthropometric indices in elderly women with NAFLD and vitamin D deficiency.

3. Methods

3.1. Design and Participants

This is a semi-experimental study with a pretest-posttest design. The study population consisted of 90 volunteers from among elderly women (60 to 65-years-old) with

NAFLD and vitamin D deficiency referring to the liver clinic of Imam Hossein Hospital in Kermanshah city, Iran. Based on the inclusion criteria, 42 women were recruited. However, two patients abandoned the study before completing the baseline procedure. The remaining 40 patients were randomly divided into four groups including aerobic training (AT, n = 10), vitamin D supplementation (Vit. D, n = 10), aerobic training with vitamin D supplementation (AT + Vit. D, n = 10), and control (C, n = 10). The inclusion criteria included an ultrasound (US) diagnosis of NAFLD (grade II or III) confirmed by an internist, 25-OHD levels between 10 and 20 ng/mL, and no specific diet and regular exercise program in the past year. The exclusion criteria included the confirmed presence of other liver diseases (hepatitis B and C), other disorders such as autoimmune hepatitis, joint disease, celiac and Wilson disease, cardiovascular disease (CVD), kidney failure, hypothyroidism, surgical treatment of obesity or severe weight loss, and the presence of any other chronic disease or skeletal disorders (3, 27).

Three days before the start of the study, the patients were explained about the research procedure and they were asked to sign consent forms. Then, they completed the physical activity readiness questionnaire (PAR-Q) and health history questionnaire (HHQ). On the first day, the height was measured using a stadiometer (DETECTO, Model 3PHTROD-WM, USA) with a sensitivity of 0.1 cm. body weight (BW), body mass index (BMI), and body fat percentage (BFP) were obtained with the INBODY test in the fasting state using bioelectric impedance analysis (Zeus 9.9 PLUS; Jawon Medical Co., Ltd., Kungsang Bukdo, South Korea). In addition, the waist-hip ratio (WHR) was measured by dividing the waist circumference by the hip circumference according to the WHO criteria. All variables were measured with the same conditions at the beginning and the end of the eight weeks of intervention.

3.2. Ethical Considerations

The present study was approved by the Ethics Committee in Research at Kermanshah University of Medical Sciences and registered at the Iranian Clinical Trial Registration Center under code IR.KUMS.REC.1397.1059. Before the study, informed written consent was obtained from all participants after a comprehensive oral and written explanation of the study was provided. All patients were allowed to leave the study at any time voluntarily. The demographic data of the participants were kept confidential. All the clinical and paraclinical tests of the study were free of charge, with no costs to the patients.

3.3. Training Program

The aerobic training program was executed three days a week for eight weeks based on the ACSM's recommendation. Each session lasted 40 - 60 minutes consisting 10 minutes of warming up, 20 to 40 minutes of aerobic exercise, and 10 minutes of cooling down. In the first week, the subjects performed 20 minutes of aerobic exercise including walking, jogging, and running at 60% HR_{max}. The duration and intensity were gradually progressed to a maximum of 40 minutes and 75% HR_{max}, respectively. The training program was performed with 60% - 75% of the individual HR_{max} and 10 - 13 of RPE using the 6 - 20 Borg scale (Table 1) (2).

3.4. Vitamin D Supplementation

In this study, both AT + Vit. D group and Vit. D group received 50,000 units of vitamin D supplement (Zahravi Pharmaceutical Company, Iran) once per week at the beginning of the week. The C and AT groups also received weekly a placebo (paraffin; Zahravi Pharmaceutical Company, Iran) similar to vitamin D supplement pills in shape, color, smell, and taste, over the period of eight weeks.

3.5. Data Analysis

The results were expressed as mean \pm SD. The differences between pretest and posttest were determined by the t test in the same group. Between-group differences were evaluated using the one-way analysis of variance (ANOVA) both before and after the intervention. Furthermore, Tukey's post hoc test was conducted if there was a significant difference between the groups. All analyses were performed using SPSS version 21.0 software at a significance level of $P < 0.05$.

4. Results

The demographic data and anthropometric indices of the participants and their between-group comparison are presented in Table 2. After eight weeks, there were significant decreases in BW, BMI, BFP, and WHR in the AT + Vit. D, AT, and Vit. D groups. However, the C group showed significant increases in BW, BMI, BFP, and WHR levels (Table 2). The results of one-way ANOVA showed no significant difference in BW, BMI, BFP, and WHR between the groups at pretest; however, significant differences were observed at posttest (Table 2).

The results of Tukey's post hoc test showed that the lowest anthropometric indices (BW, BMI, PBF, and WHR) were observed in the AT + Vit. D group. No significant difference was seen in BW, BFP, BMI, and WHR between the A +

Vit. D, AT, and Vit. D groups; however, the mentioned variables were significantly higher in the control group than in other groups at posttest (Table 2).

5. Discussion

Substantial evidence indicates that physical activity is the first-line treatment of obesity and is a management approach for obesity-related mortality and morbidity. The results of the study indicated that aerobic training alone reduced BW, BMI, BFP, and WHR; however, more reductions were observed when aerobic training was accompanied by vitamin D supplementation. Based on the results of the studies, aerobic training is associated with improvements in cardiovascular risk factors, including improved insulin resistance and weight loss (28, 29). Swift et al. found that regular exercise training increased the expression of lipolytic enzymes, the density of mitochondria, and the recruitment of fat cells instead of carbohydrates for energy demand while reduced body fat, leading to consequent reductions in BW, BMI, and BFP (30). On the other hand, the increase in anthropometric indices (BW, BMI, and WHR) is an indicator of visceral fat accumulation that has a high correlation with liver fat accumulation in NAFLD (31). Visceral fat tissues are more resistant to insulin; therefore, it might stimulate lipolysis and call for free fatty acids in the bloodstream, which is an influential factor in the accumulation of more triglycerides in the liver (32). In addition regular aerobic training is known to increase the daily energy expenditure, increase the oxidation of lipids in skeletal muscles and mitochondria of hepatocytes, and reduce the obesity, especially the abdominal obesity; they may consequently lead to reduced visceral fat, free fatty acid transfusion into the liver, and fat deposition in the liver, along with the increased fat oxidation in the liver (33, 34).

The findings of the study also showed that Vit. D alone reduced BW, BMI, and BFP. Studies report an association between vitamin D deficiency and the prevalence of chronic diseases (35, 36). Limited studies have been conducted on the relationship between vitamin D intake and BW, BMI, and BFP. Recently, Hoseini et al. reported that high doses of vitamin D could significantly reduce BW, BMI, and visceral fat in rats with metabolic syndrome (37). In a trial study, Scragg et al. compared the serum levels of 25-OHD between obese subjects and non-obese controls and reported significantly lower levels in obese subjects (38). Vitamin D is a fat-soluble vitamin that is believed to store in larger adipose tissues after synthesizing and entering the bloodstream, releasing it at a slower rate. Vitamin D concentration in fat tissue is positively correlated with its serum concentration

Table 1. Exercise Protocol Program

Variables	Weeks							
	First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth
Intensity (HR _{max}), %	60	60	65	65	70	70	75	75
Duration, min	20	25	25	30	30	35	35	40
Borg scale	10	10	11	11	11	12	12	13

Table 2. Mean \pm SD of Demographic Information and Anthropometric Indices Before the Intervention Among the Groups

Variables	AT + Vit. D (N=10)	AT (N=10)	Vit. D (N=10)	C (N=10)	P Value ^b
Age, y	63.10 \pm 2.37	62.60 \pm 1.89	61.30 \pm 1.41	62 \pm 1.88	0.16
Height, cm	157.10 \pm 5.25	160 \pm 5.45	158.30 \pm 4.59	159 \pm 5.79	0.11
Body weight, kg					
Pretest	87.40 \pm 4.64	85.80 \pm 3.35	86.10 \pm 3.14	87.50 \pm 4.19	0.679
Posttest	82.20 \pm 2.65 ^d	82.40 \pm 3.45 ^d	84 \pm 3.59 ^d	90.40 \pm 4.11	0.001 ^e
P value ^c	0.001 ^f	0.001 ^f	0.002 ^f	0.001 ^f	
BMI, kg/m²					
Pretest	35.55 \pm 3.55	33.57 \pm 1.92	34.40 \pm 1.78	34.65 \pm 1.70	0.332
Posttest	33.41 \pm 2.69 ^d	32.16 \pm 1.8 ^d	33.56 \pm 1.77 ^d	35.82 \pm 2.08	0.005 ^e
P value ^c	0.001 ^f	0.001 ^f	0.002 ^f	0.001 ^f	
Body fat percentage, %					
Pretest	44 \pm 3.36	43.10 \pm 3.41	41.20 \pm 3.15	42 \pm 3.59	0.284
Posttest	38.20 \pm 3.64 ^d	38.10 \pm 3.84 ^d	40 \pm 2.49 ^d	44.10 \pm 3.84	0.001 ^e
P value ^c	0.001 ^f	0.001 ^f	0.001 ^f	0.001 ^f	
WHR, cm					
Pretest	94.50 \pm 2.54	95.20 \pm 3.79	95.80 \pm 2.78	95.70 \pm 3.16	0.778
Posttest	89.80 \pm 1.93 ^d	93 \pm 3.36	94.40 \pm 2.95	96.40 \pm 2.83	0.001 ^e
P value ^c	0.001 ^f	0.001 ^f	0.001 ^f	0.132	

^a AT + Vit. D group, Aerobic training plus vitamin D supplementation; AT group, Aerobic training; Vit. D group, vitamin D supplementation; C group, no aerobic training and no Vit. D.

^b P values are calculated using one-way ANOVA, followed by post hoc Tukey's test.

^c P values indicates values calculated using paired t-test.

^d Significant difference between AT + Vit. D, AT, and Vit. D groups and the C group.

^e Significantly different between groups at pretest and posttest.

^f Significantly different between pretest and posttest within the groups.

(39). Contrarily, hypovitaminosis D (a decrease in vitamin D) results in the increased levels of parathyroid hormone (PTH) and intercellular Ca⁺⁺ and inhibits insulin receptors in target tissues and closes the Glut-4 channel. In addition, since insulin secretion depends on the intracellular calcium concentration, hypovitaminosis D may impair insulin function, glucose metabolism, and other metabolic processes in the adipose tissue, which might be another mechanism in the association of abdominal obesity and low levels of vitamin D (37, 40). A further reduction in anthropometric indices induced by aerobic training plus vitamin D supplementation, compared to other groups, in

the current study was probably due to the higher sensitivity of visceral adipocytes, which stimulated lipolysis in response to catecholamines. Moreover, aerobic training and vitamin D supplementation may have a direct effect on insulin sensitivity and beta cells function (14, 15). Since the increased BW, BMI, BFP, and WHR are risk factors for the development of insulin resistance, type 2 diabetes, and CVD in elderly women (8, 9), identifying the effective measures for reducing BMI, BFP, and WHR has always been a controversial issue. Further research is needed to document the vitamin D supplementation dose, training intensity, and cumulative effect of AT + Vit. D in improving anthropo-

metric indices in NAFLD patients. The limitations of this study were the use of US to detect fatty liver, instead of liver biopsy as a more accurate technique, and the small sample size due to the limited number of patients with both vitamin D deficiency and NAFLD and their age-related limitations.

5.1. Conclusions

Based on the results of this study, there are suggestions for clinicians and patients suffering from NAFLD or those who are at risk of NAFLD. Regular aerobic training is beneficial in improving the anthropometric indices and reducing the risk of NAFLD. In addition, the combined use of vitamin D supplementation and aerobic training can aggregate the beneficial effects and better reduce anthropometric indices in patients with NAFLD.

Acknowledgments

This manuscript is part of an MSc. thesis at the Department of Exercise Physiology, Faculty of Sport Sciences, Razi University, Kermanshah, Iran. The authors would like to thank the subjects for their voluntary participation in this study.

Footnotes

Authors' Contribution: Nasser Behpour participated in designing the study. Zahra Hoseini participated in the manuscript writing and data collection. Rastegar Hoseini participated in data analysis. All authors read and approved the final manuscript.

Conflict of Interests: The authors declare no competing interests.

Ethical Considerations: This study was approved by the Ethics Committee of the Kermanshah University of Medical Sciences (ID: IR.KUMS.REC.1397.1059, date: March 6, 2019).

Funding/Support: The authors declare that they received no financial support for this study and it was done by the personal budget of the corresponding author.

References

- Rinella ME. Nonalcoholic fatty liver disease: A systematic review. *JAMA*. 2015;**313**(22):2263-73. doi: [10.1001/jama.2015.5370](https://doi.org/10.1001/jama.2015.5370). [PubMed: [26057287](https://pubmed.ncbi.nlm.nih.gov/26057287/)].
- Heil DP. ACSM's guidelines for exercise testing and prescription. *Med Sci Sports Exerc*. 2001;**33**(2):343.
- Johnson NA, Sachinwalla T, Walton DW, Smith K, Armstrong A, Thompson MW, et al. Aerobic exercise training reduces hepatic and visceral lipids in obese individuals without weight loss. *Hepatology*. 2009;**50**(4):1105-12. doi: [10.1002/hep.23129](https://doi.org/10.1002/hep.23129). [PubMed: [19637289](https://pubmed.ncbi.nlm.nih.gov/19637289/)].
- Alavian SM, Ramezani M, Bazzaz A, Azuzabadi Farahani M, Behnava B, Keshvari M. [Frequency of fatty liver and some of its risk factors in asymptomatic carriers of HBV attending the Tehran blood transfusion organization hepatitis clinic]. *Iranian Journal of Endocrinology and Metabolism*. 2008;**10**(2):99-106. Persian.
- Russell-Guzmán JA, Karachon L, Gacitúa TA, Freundlich A, Poblete-Aro CE, Rodrigo R. Role of exercise in the mechanisms ameliorating hepatic steatosis in non-alcoholic fatty liver disease. *Sport Sci Health*. 2018;**14**(3):463-73. doi: [10.1007/s11332-018-0459-9](https://doi.org/10.1007/s11332-018-0459-9).
- Orci LA, Gariani K, Oldani G, Delaune V, Morel P, Toso C. Exercise-based interventions for nonalcoholic fatty liver disease: A meta-analysis and meta-regression. *Clin Gastroenterol Hepatol*. 2016;**14**(10):1398-411. doi: [10.1016/j.cgh.2016.04.036](https://doi.org/10.1016/j.cgh.2016.04.036). [PubMed: [2755553](https://pubmed.ncbi.nlm.nih.gov/2755553/)].
- Trayssac M, Hannun YA, Obeid LM. Role of sphingolipids in senescence: Implication in aging and age-related diseases. *J Clin Invest*. 2018;**128**(7):2702-12. doi: [10.1172/JCI97949](https://doi.org/10.1172/JCI97949). [PubMed: [30108193](https://pubmed.ncbi.nlm.nih.gov/30108193/)]. [PubMed Central: [PMC6025964](https://pubmed.ncbi.nlm.nih.gov/PMC6025964/)].
- Schmucker DL. Age-related changes in liver structure and function: Implications for disease? *Exp Gerontol*. 2005;**40**(8-9):650-9. doi: [10.1016/j.exger.2005.06.009](https://doi.org/10.1016/j.exger.2005.06.009). [PubMed: [16102930](https://pubmed.ncbi.nlm.nih.gov/16102930/)].
- Prestes J, Shiguemoto G, Botero JP, Frollini A, Dias R, Leite R, et al. Effects of resistance training on resistin, leptin, cytokines, and muscle force in elderly post-menopausal women. *J Sports Sci*. 2009;**27**(14):1607-15. doi: [10.1080/02640410903352923](https://doi.org/10.1080/02640410903352923). [PubMed: [19967592](https://pubmed.ncbi.nlm.nih.gov/19967592/)].
- Hallsworth K, Fattakhova G, Hollingsworth KG, Thoma C, Moore S, Taylor R, et al. Resistance exercise reduces liver fat and its mediators in non-alcoholic fatty liver disease independent of weight loss. *Gut*. 2011;**60**(9):1278-83. doi: [10.1136/gut.2011.242073](https://doi.org/10.1136/gut.2011.242073). [PubMed: [21708823](https://pubmed.ncbi.nlm.nih.gov/21708823/)]. [PubMed Central: [PMC3152868](https://pubmed.ncbi.nlm.nih.gov/PMC3152868/)].
- Kawanishi N, Yano H, Mizokami T, Takahashi M, Oyanagi E, Suzuki K. Exercise training attenuates hepatic inflammation, fibrosis and macrophage infiltration during diet induced-obesity in mice. *Brain Behav Immun*. 2012;**26**(6):931-41. doi: [10.1016/j.bbi.2012.04.006](https://doi.org/10.1016/j.bbi.2012.04.006). [PubMed: [22554494](https://pubmed.ncbi.nlm.nih.gov/22554494/)].
- Davoodi M, Moosavi H, Nikbakht M. [The effect of eight weeks selected aerobic exercise on liver parenchyma and liver enzymes (AST, ALT) of fat liver patients]. *J Shahrekord Univ Med Sci*. 2012;**14**(1):84-90. Persian.
- Devries MC, Samjoo IA, Hamadeh MJ, Tarnopolsky MA. Effect of endurance exercise on hepatic lipid content, enzymes, and adiposity in men and women. *Obesity (Silver Spring)*. 2008;**16**(10):2281-8. doi: [10.1038/oby.2008.358](https://doi.org/10.1038/oby.2008.358). [PubMed: [18719669](https://pubmed.ncbi.nlm.nih.gov/18719669/)].
- Holick MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. *Rev Endocr Metab Disord*. 2017;**18**(2):153-65. doi: [10.1007/s11154-017-9424-1](https://doi.org/10.1007/s11154-017-9424-1). [PubMed: [28516265](https://pubmed.ncbi.nlm.nih.gov/28516265/)].
- Holick MF, Chen TC. Vitamin D deficiency: A worldwide problem with health consequences. *Am J Clin Nutr*. 2008;**87**(4):1080S-6S. doi: [10.1093/ajcn/87.4.1080S](https://doi.org/10.1093/ajcn/87.4.1080S). [PubMed: [18400738](https://pubmed.ncbi.nlm.nih.gov/18400738/)].
- Vatandost S, Jahani M, Afshari A, Amiri MR, Heidarimoghadam R, Mohammadi Y. Prevalence of vitamin D deficiency in Iran: A systematic review and meta-analysis. *Nutr Health*. 2018;**2**:6010601880297E+14. doi: [10.1177/0260106018802968](https://doi.org/10.1177/0260106018802968). [PubMed: [30296903](https://pubmed.ncbi.nlm.nih.gov/30296903/)].
- Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M, et al. Vitamin D deficiency and causative factors in the population of Tehran. *BMC Public Health*. 2004;**4**:38. doi: [10.1186/1471-2458-4-38](https://doi.org/10.1186/1471-2458-4-38). [PubMed: [15327695](https://pubmed.ncbi.nlm.nih.gov/15327695/)]. [PubMed Central: [PMC517720](https://pubmed.ncbi.nlm.nih.gov/PMC517720/)].
- Saki F, Dabbaghmanesh MH, Omrani GR, Bakhshayeshkaram M. Vitamin D deficiency and its associated risk factors in children and adolescents in southern Iran. *Public Health Nutr*. 2017;**20**(10):1851-6. doi: [10.1017/S1368980015001925](https://doi.org/10.1017/S1368980015001925). [PubMed: [26051113](https://pubmed.ncbi.nlm.nih.gov/26051113/)].

19. He X, Shen Y, Ma X, Ying L, Peng J, Pan X, et al. The association of serum FGF23 and non-alcoholic fatty liver disease is independent of vitamin D in type 2 diabetes patients. *Clin Exp Pharmacol Physiol*. 2018;**45**(7):668–74. doi: [10.1111/1440-1681.12933](#). [PubMed: [29574933](#)].
20. González-Rodríguez Á, Petrov P, Pozo-Maroto ED, Guzmán C, de Cía JR, Vargas-Castrillón J, et al. Angiopoietin-like protein 8 is a novel vitamin D receptor-targeted lipogenic gene associated with non-alcoholic fatty liver. *J Hepatol*. 2018;**68**:S361–2. doi: [10.1016/s0168-8278\(18\)30948-6](#).
21. Leung PS. The potential protective action of vitamin D in hepatic insulin resistance and pancreatic islet dysfunction in type 2 diabetes mellitus. *Nutrients*. 2016;**8**(3):147. doi: [10.3390/nu8030147](#). [PubMed: [26959059](#)]. [PubMed Central: [PMC4808876](#)].
22. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;**67**(1):328–57. doi: [10.1002/hep.29367](#). [PubMed: [28714183](#)].
23. McGill AT, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. *Nutr J*. 2008;**7**:4. doi: [10.1186/1475-2891-7-4](#). [PubMed: [18226257](#)]. [PubMed Central: [PMC2265738](#)].
24. Tabesh M, Callegari ET, Gorelik A, Garland SM, Nankervis A, Subasinghe AK, et al. Associations between 25-hydroxyvitamin D levels, body composition and metabolic profiles in young women. *Eur J Clin Nutr*. 2018;**72**(8):1093–102. doi: [10.1038/s41430-018-0086-1](#). [PubMed: [29367732](#)].
25. Rocha R, Cotrim HP, Carvalho FM, Siqueira AC, Braga H, Freitas LA. Body mass index and waist circumference in non-alcoholic fatty liver disease. *J Hum Nutr Diet*. 2005;**18**(5):365–70. doi: [10.1111/j.1365-277X.2005.00634.x](#). [PubMed: [16150132](#)].
26. Cheung O, Kapoor A, Puri P, Sistrun S, Luketic VA, Sargeant CC, et al. The impact of fat distribution on the severity of nonalcoholic fatty liver disease and metabolic syndrome. *Hepatology*. 2007;**46**(4):1091–100. doi: [10.1002/hep.21803](#). [PubMed: [17610277](#)].
27. Al-Jiffri O, Al-Sharif FM, Abd El-Kader SM, Ashmawy EM. Weight reduction improves markers of hepatic function and insulin resistance in type-2 diabetic patients with non-alcoholic fatty liver. *Afr Health Sci*. 2013;**13**(3):667–72. doi: [10.4314/ahs.v13i3.21](#). [PubMed: [24250305](#)]. [PubMed Central: [PMC3824460](#)].
28. ten Brinke LF, Hsu CL, Best JR, Barha CK, Liu-Ambrose T. Increased aerobic fitness is associated with cortical thickness in older adults with mild vascular cognitive impairment. *J Cogn Enhanc*. 2018;**2**(2):157–69. doi: [10.1007/s41465-018-0077-0](#).
29. Fiuza-Luces C, Santos-Lozano A, Joyner M, Carrera-Bastos P, Picazo O, Zugaza JL, et al. Exercise benefits in cardiovascular disease: Beyond attenuation of traditional risk factors. *Nat Rev Cardiol*. 2018;**15**(12):731–43. doi: [10.1038/s41569-018-0065-1](#). [PubMed: [30115967](#)].
30. Swift DL, Johannsen NM, Lavie CJ, Earnest CP, Church TS. The role of exercise and physical activity in weight loss and maintenance. *Prog Cardiovasc Dis*. 2014;**56**(4):441–7. doi: [10.1016/j.pcad.2013.09.012](#). [PubMed: [24438736](#)]. [PubMed Central: [PMC3925973](#)].
31. Church TS, Kuk JL, Ross R, Priest EL, Biloft E, Blair SN. Association of cardiorespiratory fitness, body mass index, and waist circumference to nonalcoholic fatty liver disease. *Gastroenterology*. 2006;**130**(7):2023–30. doi: [10.1053/j.gastro.2006.03.019](#). [PubMed: [16762625](#)].
32. Chen ZW, Chen LY, Dai HL, Chen JH, Fang LZ. Relationship between alanine aminotransferase levels and metabolic syndrome in non-alcoholic fatty liver disease. *J Zhejiang Univ Sci B*. 2008;**9**(8):616–22. doi: [10.1631/jzus.B0720016](#). [PubMed: [18763311](#)]. [PubMed Central: [PMC2491691](#)].
33. Smart NA, King N, McFarlane JR, Graham PL, Dieberg G. Effect of exercise training on liver function in adults who are overweight or exhibit fatty liver disease: A systematic review and meta-analysis. *Br J Sports Med*. 2018;**52**(13):834–43. doi: [10.1136/bjsports-2016-096197](#). [PubMed: [27317790](#)]. [PubMed Central: [PMC6029644](#)].
34. van der Windt DJ, Sud V, Zhang H, Tsung A, Huang H. The effects of physical exercise on fatty liver disease. *Gene Expr*. 2018;**18**(2):89–101. doi: [10.3727/105221617X15124844266408](#). [PubMed: [29212576](#)]. [PubMed Central: [PMC5954622](#)].
35. Schiller A, Gadalean F, Schiller O, Timar R, Bob F, Munteanu M, et al. Vitamin D deficiency-prognostic marker or mortality risk factor in end stage renal disease patients with diabetes mellitus treated with hemodialysis—a prospective multicenter study. *PLoS One*. 2015;**10**(5):e0126586. doi: [10.1371/journal.pone.0126586](#). [PubMed: [25965403](#)]. [PubMed Central: [PMC4428845](#)].
36. Zhang MX, Pan GT, Guo JF, Li BY, Qin LQ, Zhang ZL. Vitamin D deficiency increases the risk of gestational diabetes mellitus: A meta-analysis of observational studies. *Nutrients*. 2015;**7**(10):8366–75. doi: [10.3390/nu7105398](#). [PubMed: [26437429](#)]. [PubMed Central: [PMC4632418](#)].
37. Hoseini R, Babaei P, Damirchi A. [The effect of different doses of vitamin D supplementation on insulin resistance in ovariectomized rats]. *J Birjand Univ Med Sci*. 2016;**23**(1):11–20. Persian.
38. Scragg R, Sowers M, Bell C, Third National H, Nutrition Examination S. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. *Diabetes Care*. 2004;**27**(12):2813–8. doi: [10.2337/diacare.27.12.2813](#). [PubMed: [15562190](#)].
39. Blum M, Dolnikowski G, Seyoum E, Harris SS, Booth SL, Peterson J, et al. Vitamin D(3) in fat tissue. *Endocrine*. 2008;**33**(1):90–4. doi: [10.1007/s12020-008-9051-4](#). [PubMed: [18338271](#)]. [PubMed Central: [PMC2839878](#)].
40. Babaei P, Damirchi A, Hoseini R. The interaction effects of aerobic exercise training and vitamin D supplementation on plasma lipid profiles and insulin resistance in ovariectomized rats. *J Exerc Nutrition Biochem*. 2015;**19**(3):173–82. doi: [10.5717/jenb.2015.15070703](#). [PubMed: [26526941](#)]. [PubMed Central: [PMC4624118](#)].