Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1524634
J Health Sci Med. 2024;7(5):524-528

Relationship between 25(OH)D3 levels and cognitive functions in children with obesity

Samet Özer[1], Hasan Bozkurt[2], İlknur Bütün[3]
[1]*Department of Pediatrics, Hüma International Hospital, Kayseri, Turkiye*
[2]*Department of Child and Adolescent Psychiatry, A Life Hospital, Ankara, Turkiye*
[3]*Department of Medical Biochemistry, Faculty of Medicine, Gaziosmanpaşa University, Tokat, Turkiye*

Cite this article as: Özer S, Bozkurt H, Bütün İ. Relationship between 25(OH)D3 levels and cognitive functions in children with obesity. *J Health Sci Med.* 2024;7(5):524-528.

Received: 02.08.2024 ◆ **Accepted**: 24.08.2024 ◆ **Published**: 27.09.2024

ABSTRACT

Aims: The inconsistent results about neurocognitive functions in children with obesity may be suggestive of factors like vitamin deficiencies rather than the disorder itself. So we aimed to investigate the 25(OH)D3 levels and cognitive functions in obese children in the present study.

Methods: Seventy-two children were included to this study. Forty-one of them were obese children and 31 children were with normal weight. The patients were diagnosed as obese according to body mass index >95 percentile, considering the sex and age-specific growth curves for Turkish children. The participants completed the battery tests of the central nervous system vital signs (CNSVS), a neurocognitive test battery, via computer. The battery calculates seven domain scores (Memory, Psychomotor speed, Processing speed, Reaction time, Complex attention, Executive function, Cognitive flexibility) and a summary score (Neurocognition Index). 25(OH)D3 levels were measured in residual samples using a Shimadzu HPLC system with the aid of a 25(OH)D3 kit. The scores were compared by using commercial software (IBM SPSS Statistics 18).

Results: The mean 25-OH-vitamin D levels were 13.41±7.91 µg/L in obese children and 20.31±5.92µg/L in controls. Vitamin D3 levels were significantly lower in obese children than in control group ($p<0.05$). There was statistically significant difference between patient and healthy control group on all cognitive performance domains. Mean NCI score of obesity group was 86.17±8.85, whereas that of healthy participants was 90.61±8.28. The mean NCI score in the obesity group was significantly lower than that of the control group ($p<0.001$).

Conclusion: Cognitive index of obese children is lower than normal weight children. Lower 25(OH)D3 levels are related to cognitive deficits in children with obesity. Cognitive dysfunction and 25(OH)D3 levels in obese children and adolescents should be addressed in the evaluation and treatment of this population.

Keywords: Child, obesity, 25-OH-vitamin D, cognitive dysfunction

INTRODUCTION

The prevalence of childhood obesity has increased dramatically and steadily in last four decades and obesity has become a serious worldwide public health problem. Obesity is not only an increased calorie intake and weight management problem, but also a malnutrition condition with vitamin deficiency and reduce in cognitive functions.[1,2] It is well known that vitamin D insufficiency is more prevalent in children with obesity.[3-5] Etiopathogenesis of vitamin D deficiency in obese children is not clear. Some investigators claimed that the sequestration of vitamin D in the body fat and its consequent is reduced bioavailability, others claimed that fewer outdoor activities and reduced sunlight exposure contributes to reduced endogenous vitamin D production.[6]

Recent studies investigated executive cognitive functions in obesity. A negative relationship between body-mass index (BMI) and neurocognitive performance in adults has been shown in many studies in the literature.[7] Cognitive dysfunction generally refers to deficits in memory and executive function, and many diseases other than obesity may show cognitive dysfunction.[8] Cognitive dysfunction associated with high calorie intake and sedanter behaviour and negatively associated with fruit and vegetable intake and physical activity, briefly associated with obesity.[9] It is shown that improvements in executive functions were also found to be related to weight loss suggesting that neurocognitive functions have positive implications for reducing weight in obese adolescents.[10] Some investigators suggested that inflammation is the underlying mechanism of cognitive deficit related to obesity.[11] It is shown that reducing inflammation by vitamin D contributes the development of cognitive functions in rat model.[12] Vitamin D is not only involved in bone metabolism. Recent studies have demonstrated that vitamin D is a neuro-protective and an

Corresponding Author: Samet Özer, sozerdr@hotmail.com

anti-inflammatory biologic agent.[13] VDR have been located in cortex, cerebellum, thalamus, hypothalamus, basal ganglions and hippocampus. Some of these areas are regulating cognitive functions and absence of the VDR has been associated with neurodegenerative diseases.[14,15] Therefore, we aimed to investigate the relationship between 25-OH-vitamin D levels and cognitive functions in children with obesity.

METHODS

Participants

In the present study 72 children were included. Forty one of them were obese and others were normal weight. The patients were diagnosed as obese according to BMI >95 percentil, considering the sex and age-specific growth curves for Turkish children.[16] Weights were measured with digital scale (Seca). Measurements were done while patients are barefoot and light cloth wearing. Height was measured with portable stadiometer (Harpenden). BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Subjects with any genetic syndrome, metabolic (e.g., type 2 diabetes, metabolic syndrome) or endocrine disease (e.g., Cushing syndrome, hypothyroidism) and other diseases (e.g., hypertension, non-alcoholic fatty liver disease) as well as subjects on medications or a diet were excluded. All children and adolescents in the obesity and control groups with an IQ<80 on the fifth edition of the Stanford-Binet intelligence test, and with a diagnosis of any neurological disorder or head injury, and color blindness, past or current substance abuse were excluded from the study. The study protocol was approved by the Non-invasive Clinical Research Ethics Committee of Gaziosmanpaşa University (Date: 30.03.2016, Decision No: 16-KAEK-073) and written informed consent was obtained from both parents before starting any study-related procedure. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Measures

Central nervous system vital signs (CNSVS): The CNSVS is a computerized, neurocognitive test battery for use in clinical research. The psychometric characteristics of the tests in the CNSVS battery are very similar to the characteristics of the conventional neuropsychological tests and the reliability and validity has been demonstrated.[17] It has normative data for children as young as 7 years of age and Cohen d effect sizes range from d=0.44 to d=1.19 regarding retest reliability in children and adolescents.[18] It is administered via a computer and takes approximately 30 to 40 minutes to complete. The CNSVS comprises of 7 common neuropsychological measures: verbal memory test, visual memory test, finger tapping test (FTT), symbol digit coding (SDC), the stroop test (ST), shifting attention test (SAT) and continuous performance test (CPT). The battery generates 15 primary scores which are used to calculate seven domain scores (Memory, Psychomotor speed, Processing speed, Reaction time, Complex attention, Executive Function, and Cognitive flexibility) and a summary score (Neurocognition Index). Domain scores are presented as index scores, with a mean of 100 and standard deviation (SD) of 15.

Laboratory test: Blood samples were drawn for routine testing and 25-OH-vitamin D levels were measured in residual samples using a Shimadzu HPLC system (Shimadzu Corp. Kyoto, Japan) with the aid of a 25-OH-vitamin D kit (Recipe Chemicals +Instruments GmbH, Munich, Germany).

RESULTS

The study group consisted of 41 patients (19 males, 22 females) with a mean age of 11.85±2.43 years of age. Thirty one healthy children and adolescents (15 males, 16 females) with a mean age of 11.9±2.96 years were included in the control group. There is no statistically significant difference between groups in terms of number, gender, and age of the participants (p>0.05). Demographic, laboratory and clinical findings are shown in Table 1. The mean 25-OH-vitamin D levels were 13.41±7.91 µg/L in obese children and 20.31±5.92µg/L in controls. Vitamin D levels were significantly lower in obese children than in control group (p<0.001).

Table 1. Comparison of cognitive functions and vitamin D3 status between obese children and healthy control

Variables	Group			Bonferoni 95% CI	
	Patients n: 41 Mean±SD	Healthy n: 31 Mean±SD	p	Lower	Upper
Gender (male/female)	19/22	15/16	0.863	-	-
Age (years)	12.15±1.75	12.39±2.47	0.630	-	-
BMI	29.27±4.00	20.70±3.65	<0.001	-	-
BMI-SDS	2.74±0.39	1.25±0.24	<0.001	-	-
25(-OH) D3 (ng/ml)	13.41±7.91	20.31±5.92	<0.001	-	-
Calcium (mg/dl)	9.96±0.31	9.84±0.30	0.128	-	-
Phosphate (mg/dl)	4.54±0.59	4.59±0.50	0.747	-	-
ALP	209.98±92.14	224.27±99.43	0.551	-	-
NCI	86.17±8.85	90.61±8.28	0.034	-1.50	10.38
Composite memory	86.22±10.45	95.1±10.65	0.001	1.61	16.15
Verbal memory	87.44±10.30	98.87±12.37	<0.001	3.68	19.18
Visual memory	89.51±12.18	96.65±9.38	0.009	-0.50	14.77
Processing Speed	88.29±12.78	96.94±8.88	0.002	0.86	16.42
Executive function	89.24±11.32	93.32±10.11	0.118	-3.38	11.54
Psychomotor speed	87.98±12.18	94.13±6.96	0.009	-0.93	13.24
Reaction time	77.37±14.64	90.52±18.55	0.001	1.81	24.49
Complex attention	90.37±9.72	98.74±8.65	<0.001	1.98	14.78
Cognitive flexibility	88.54±10.26	93.29±10.03	0.053	-2.26	11.76

p1: Individual t-test significance levels, p2: Hotelling's T2 test (Multivariate analysis) was used, SD: Standard deviation, BMI: Body-mass index, BMI SDS: Body-mass index standard deviation score

The two groups were compared on the 7 index scores of CNSVS. There was statistically significant difference between patient and healthy control group on all cognitive performance domains. Mean NCI score of obesity group was 86.17±8.85, whereas that of healthy participants was 90.61±8.28 (p:0.034). The mean score of NCI in patients with obesity was significantly lower than that of healthy control

participants by calculating according to one variable analysis. But the statistically importance got lost when the data were calculated according to multiple variable analysis Bonferroni test. The same results were seen when evaluating the visual memory, executive function and psychomotor speed. But the mean scores of composite memory, verbal memory, processing speed, reaction time and complex attention were statistically different among the healthy subjects and obese children according to results of one variable test and multiple variable tests Bonferroni. Table 1 shows the scores for group differences in cognitive performance of obesity and matched control group.

Mean cognitive index was similar in groups girls and boys (p=0.232). Vitamin D levels belong to patients were significantly lower than control group (p<0.001). Lower cognitive indexes were significantly in a correlation with lower vitamin D levels. The most effected function is verbal memory. Reaction time shows no difference between obese patients and control group.

According to regression analysis for 25(OH)D3 a 0.01 µg/L increase in 25(OH)D3 level provides an increase of 0.167 units in NCI, but this increase is not statistically significant (t=1.301: p=0.197). Similar results were revealed by the regression test from the other parameters for CNSVS. In the regression analysis performed according to vitamin D levels and the study group, the change in NCI of obese children is 0.178 units less than healthy children, but this decrease is not statistically significant (t=-1.391: p=0.169) (Table 2).

Table 2. Regression results for 25-(OH)-D3 and study group independent predictors on CNSVS parameters

Predictors	CNSVS parameters	β	t	p
Obese	NCI	0.167	1.301	0.197
Healthy		-0.178	-1.391	0.169
Obese	Composite memory	-0.161	-1.325	0.189
Healthy		-0.460	-3.781	<0.001
Obese	Verbal memory	-0.190	-1.628	0.411
Healthy		-0.538	-4.602	0.026
Obese	Visual memory	0.043	0.337	0.737
Healthy		-0.289	-2.272	0.026
Obese	Processing speed	-0.231	-1.897	0.062
Healthy		-0.460	-3.779	<0.001
Obese	Executive function	-0.048	-0.366	0.716
Healthy		-0.207	-1.576	0.120
Obese	Psychomotor speed	0.182	1.442	0.154
Healthy		-0.208	-1.651	0.103
Obese	Reaction time	0.124	1.007	0.317
Healthy		-0.319	-2.584	0.012
Obese	Complex attention	-0.082	-0.678	0.500
Healthy		-0.449	-3.695	<0.001
Obese	Cognitive flexibility	-0.055	-0.424	0.673
Healthy		-0.253	-1.943	0.056

CNSVS Central nervous system vital signs

DISCUSSION

The study investigated the relationship between 25-OH-vitamin D levels and cognitive functions in children with obesity. The results show that the children with obesity performed significantly worse than non-obese healthy controls on all cognitive domains. This present study is also important for evaluating 25-OH-vitamin D levels along with neurocognitive functions comparing them with those of a control group.

Childhood obesity is a growing serious health problem all over the world. It is giving rise to devastating public health issues together and threatening the child health. Also governments take into account the economic magnitude while struggling to recover deleterious effects of obesity [19]. Obesity is not only eating or getting more calorie disorder but also genetic, metabolic and systematic disease. We can meet health problems in many organs and organ systems. Mental health is also affected by obesity induced oxidative stress. It is well known that in various mechanisms obesity induces systemic oxidative stress resulting cognitive impairments. Obesity usually correlates with increased prevalence of vitamin deficiencies or decreased circulating 25(OH)D3 levels. Lower serum 25(OH)D3 levels were associated with higher BMI and metabolic syndrome parameters. Various studies have demonstrated that obese people have lower 25(OH)D3 levels than normal weight people. Synthesis and regulation of 25(OH) D3 confirmed that obese patients had lower basal 25(OH)D3 levels and higher serum parathyroid hormone levels than non-obese patients.[20] In many studies it is shown that vitamin D levels were lower in obese children than normal weights. Some theories are put forward to explain the relationship between lower vitamin D levels and obesity. One of them is volumetric dilution of vitamin D is probable mechanism of the inverse relationship between vitamin D serum levels and BMI.[21] The most popular accepted physiopathologic mechanism of low vitamin D level is that vitamin D, being fat-soluble, is over-absorbed by adipose tissue. Fiamenghi has conducted a study as a meta-analysis including 24,600 patients and confirmed that obesity is in a strong relationship between lower vitamin D levels as demonstrated in this study.[22] In a systematic review exploring the association between obesity and Vitamin D levels demonstrated that obese subjects have lower vitamin D levels than normal and overweight group.[23]

Chronic inflammation, endothelial dysfunction, and mitochondrial dysfunction are the sample mechanisms of the oxidative stress effects in obese population.[24] A study conducted by Li et al.[25] comparing the cognitive ability in overweight and healthy children demonstrated that the cognitive ability is lower in overweight group. On the other hand overweight or obese children show no difference in terms of cognitive ability in healthy children with normal BMI.[26] But it should also be noted that the number of these studies is limited. Obese children were also more likely to have low school success, psychosocial problems like social marginalization and low self-esteem.[27] The findings of this study that obese children have reduced cognitive functioning are consistent with the growing number of studies linking obesity and poor neurocognitive outcome.

We also found lower serum 25-OH-vitamin D levels in obese children in the present study.

There have been many biologically relevant receptors for vitamin D found in many cells, including neurons and glial cells. In humans, vitamin D is a neuro-steroid hormone that can regulate muscle function, neuro-protection, neuro-immunomodulation, and brain function. Human cortex and hippocampus areas are very important for cognition and vitamin D receptors (VDR) are especially located in these areas. Harse et al.[28] demonstrated that the higher 25-OH-vitamin D concentrations were found to be associated with increased cognitive performance in their meta analyse study.

In the present study, we aim to answer why cognitive disability is observed in some obese children but not in normal-weight children. We investigate the relationship between obesity, low cognitive performance, and lower vitamin D levels. We demonstrated a strong relationship between obesity, low vitamin D levels, and poor cognitive performance in children. Guo et al.[29] demonstrated an important relationship between lower vitamin D levels and cognitive impairment as we point out in this study. Furthermore Almuqbil et al.[30] also showed that vitamin D deficiency is related to depression, stress and anxiety which can lead to cognitive impairment in university students. A meta-analysis revealed that people with high vitamin D levels had better cognitive functions than those with low vitamin D levels. Another study conducted with mice showed that Vitamin D suppressed inflammation in the hippocampus explaining the improved cognitive functions in these mice.[31] Studies have indicated that vitamin D protects against memory dysfunction caused by oxidative stress and inflammation in the hippocampus by suppressing TNF-α. and stimulating vitamin D receptors. Additionally, a study showed that serum 25(OH)D3 levels were inversely associated with systemic inflammation biomarkers in obese people.[32] Literature supports the findings of the present study.

Limitations

Our study has several limitations that should be addressed. Firstly we didn't control for socio-economic status (household income, parental education, etc.) in our population. Because obesity is strongly associated with poverty, which is itself a significant risk factor for cognitive dysfunction. Moreover, the deficits on cognition measured by computerized battery should be supported with conventional neuropsychological tests for exact measuring. Another important limitation of this study is that it did not monitor the extent to which cognitive functions improved after vitamin D treatment in children with cognitive dysfunction and low vitamin D levels.

CONCLUSION

Vitamin D levels are significantly lower in obese individuals compared to the normal population. Concurrently, significant cognitive dysfunction is observed in obese individuals. According to the data obtained from this study, one of the important reasons for cognitive dysfunction in obese individuals is the low vitamin D levels caused by obesity. Further research should be conducted with a larger study group to reveal the expected improvement in cognitive functions following vitamin D treatment.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Gaziosmanpaşa University Faculty of Medicine Clinical Researches Ethics Committee (Date: 30.03.2016, Decision No: 16-KAEK-073).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Weiss R, Bremer AA, Lustig RH. What is metabolic syndrome, and why are children getting it? *Ann N Y Acad Sci.* 2013;1281(1):123-140. doi:10.1111/nyas.12030
2. Gobato AO, Vasques AC, Zambon MP, Barros Filho Ade A, Hessel G. Metabolic syndrome and insulin resistance in obese adolescents. *Rev Paul Pediatr.* 2014;32(1):55-62.
3. Andıran N, Çelik N, Akça H, Doğan G. Vitamin D deficiency in children and adolescents. *J Clin Res Pediatr Endocrinol.* 2012;4(1):25-29. doi:10.4274/jcrpe.574
4. Plesner JL, Dahl M, Fonvig CE, et al. Obesity is associated with vitamin D deficiency in Danish children and adolescents. *J Pediatr Endocrinol Metab.* 2018;31(1):53-61. doi:10.1515/jpem-2017-0246
5. Lagunova Z, Porojnicu AC, Lindberg FA, Aksnes L, Moan J. Vitamin D status in Norwegian children and adolescents with excess body weight. *Pediatr Diabetes.* 2011;12(2):120-126. doi:10.1111/j.1399-5448.2010.00672.x
6. Rajakumar K, Fernstrom JD, Holick MF, Janosky JE, Greenspan SL. Vitamin D status and response to vitamin D (3) in obese vs. non-obese African American children. *Obesity (Silver Spring).* 2008;16(1):90-95. doi:10.1038/oby.2007.23
7. Dye L, Boyle NB, Champ C, Lawton C. The relationship between obesity and cognitive health and decline. *Proc Nutr Soc.* 2017;76(4):443-454. doi:10.1017/S0029665117002014
8. Davis CL, Tomporowski PD, Boyle CA, et al. Effects of aerobic exercise on overweight children's cognitive functioning: a randomized controlled trial. *Res Q Exerc Sport.* 2007;78(5):510-519. doi:10.1080/02701367.2007.10599450
9. Ronan L, Alexander-Bloch A, Fletcher PC. Childhood obesity, cortical structure, and executive function in healthy children. *Cereb Cortex.* 2020;30(4):2519-2528. doi: 10.1093/cercor/bhz257
10. Staiano AE, Abraham AA, Calvert SL. Competitive versus cooperative exergame play for African American adolescents' executive function skills: short-term effects in a long-term training intervention. *Dev Psychol.* 2012;48(2):337-342.

11. Reger MA, Watson GS, Frey WH 2nd, et al. Effects of intranasal insulin on cognition in memory-impaired older adults: modulation by APOE genotype. *Neurobiol Aging.* 2006;27(3):451-458. doi:10.1016/j.neurobiolaging.2005.03.016
12. Erbaş O, Solmaz V, Aksoy D, Yavaşoğlu A, Sağcan M, Taşkıran D. Cholecalciferol (vitamin D 3) improves cognitive dysfunction and reduces inflammation in a rat fatty liver model of metabolic syndrome. *Life Sci.* 2014;103(2):68-72. doi:10.1016/j.lfs.2014.03.035
13. Argano C, Mirarchi L, Amodeo S, Orlando V, Torres A, Corrao S. The role of vitamin D and its molecular bases in insulin resistance, diabetes, metabolic syndrome, and cardiovascular disease: state of the art. *Int J Mol Sci*. 2023;24(20):15485. doi:10.3390/ijms242015485
14. Annweiler C, Allali G, Allain P, et al. Vitamin D and cognitive performance in adults: a systematic review. *Eur J Neurol.* 2009;16(10):1083-1089. doi:10.1111/j.1468-1331.2009.02755.x
15. Yılmaz M, Yılmaz N. D Vitaminin beyindeki rolü ve ilişkili nörolojik hastalıklar. *J Clin Exp Invest.* 2013.4(3).
16. Neyzi O, Günöz H, Furman A, et al. Türk çocuklarinda vücut ağırlığı, boy uzunluğu, baş çevresi ve vücut kitle indeksi referans değerleri. *Çocuk Sağ Hast Derg.* 2008;51:1-14.
17. Gualtieri CT, Johnson LG. Reliability and validity of a computerized neurocognitive test battery, CNS vital signs. *Arch Clin Neuropsychol.* 2006;21(7):623-643. doi: 10.1016/j.acn.2006.05.007
18. Brooks BL, Holdnack JA, Iverson GL. Reliable change on memory tests is common in healthy children and adolescents. *Arch Clin Neuropsychol.* 2017;32(8):1001-1009. doi: 10.1093/arclin/acx028
19. Rosengren A, Teo K, Rangarajan S, et al. Psychosocial factors and obesity in 17 high-, middle- and low-income countries: the prospective urban rural epidemiologic study. *Int J Obes (Lond).* 2015;39(8):1217-1223. doi:10.1038/ijo.2015.48
20. Tosunbayraktar G, Bas M, Kut A, Buyukkaragoz AH. Low serum 25 (OH) D levels are associated to hıgher BMI and metabolic syndrome parameters in adult subjects in Turkey. *Afr Health Sci.* 2015;15(4):1161-1169. doi:10.4314/ahs.v15i4.15
21. Vranić L, Mikolašević I, Milić S. Vitamin D deficiency: consequence or cause of obesity? *Medicina (Kaunas).* 2019;55(9):541. doi: 10.3390/medicina55090541
22. Fiamenghi VI, Mello ED. Vitamin D deficiency in children and adolescents with obesity: a meta-analysis. *J Pediatr (Rio J).* 2021;97(3):273-279. doi: 10.1016/j.jped.2020.08.006
23. Pereira-Santos M, Costa PR, Assis AM, Santos CA, Santos DB. Obesity and vitamin D deficiency: a systematic review and meta-analysis. *Obes Rev.* 2015;16(4):341-349. doi:10.1111/obr.1223924
24. Grasemann H, Holguin F. Oxidative stress and obesity-related asthma. *Paediatr Respir Rev.* 2021;37:18-21. doi: 10.1016/j.prrv.2020.05.004
25. Li Y, Dai Q, Jackson JC, Zhang J. Overweight is associated with decreased cognitive functioning among school-age children and adolescents. *Obesity (Silver Spring).* 2008;16(8):1809-1815. doi:10.1038/oby.2008.296
26. Halfon N, Larson K, Slusser W. Associations between obesity and comorbid mental health, developmental, and physical health conditions in a nationally representative sample of US children aged 10 to 17. *Acad Pediatr.* 2013;13(1):6-13. doi: 10.1016/j.acap.2012.10.007
27. Liang J, Matheson BE, Kaye WH, Boutelle KN. Neurocognitive correlates of obesity and obesity-related behaviors in children and adolescents. *Int J Obes (Lond).* 2014;38(4):494-506.
28. Harse JD, Marriott RJ, Zhu K, Murray K, Bucks RS. Vitamin D status and cognitive performance in community-dwelling adults: a dose-response meta-analysis of observational studies. *Front Neuroendocrinol.* 2023;70:101080. doi:10.1016/j.yfrne.2023.101080
29. Guo J, Mo H, Zuo L, Zhang X. Association of physical activity and vitamin D deficiency with cognitive impairment in older adults: a population based cross-sectional analysis. *Front Nutr.* 2024;11:1390903. doi:10.3389/fnut.2024.1390903
30. Almuqbil M, Almadani ME, Albraiki SA, et al. Impact of vitamin D deficiency on mental health in university students: a cross-sectional study. *Healthcare (Basel).* 2023;11(14):2097. doi:10.3390/healthcare11142097
31. Tan X, Gao L, Cai X, et al. Vitamin D3 alleviates cognitive impairment through regulating inflammatory stress in db/db mice. *Food Sci Nutr.* 2021;9(9):4803-4814. doi:10.1002/fsn3.2397
32. Xie Y, Bai C, Feng Q, Gu D. Serum vitamin D3 concentration, sleep, and cognitive impairment among older adults in China *Nutrients.* 2023;15(19):4192. doi:10.3390/nu15194192