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Original article

Effect of walking exercise on liver enzymes in children with phenylketonuria and non-alcoholic fatty liver disease: A randomized controlled trial

Efecto del ejercicio de caminar sobre las enzimas hepáticas en niños con fenilcetonuria y enfermedad del hígado graso no alcohólico: ensayo aleatorizado

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ABSTRACT

Background: Phenylketonuria (PKU), the inherited metabolic autosomal recessive disorder, is a prevalent disorder in Arabic countries (1 in 6000 babies are affected by this disorder) due to the high prevalence of consanguinity. In children with PKU, excess body weight and its associated complications – such as non-alcoholic fatty liver disease (NAFLD) – are highly reported due to the sedentary lifestyle, low physical activity, and restriction of the consumption of most important natural dietary proteins that can pose a potential risk of overconsumption of carbohydrates, sugars, and fats to meet children's energy needs. Investigating the effect of an 8-week walking exercise program on liver enzymes in children with PKU and NAFLD was the aim of this randomized controlled trial.

Methods: This PKU trial is a randomized controlled trial in children. Forty overweight/obese children with PKU and NAFLD who were aged 9–12 years old were included. Children were randomly assigned into an exercise group ($n = 20$) that received an 8-week free walking program or control group (waitlist group, $n = 20$). Serum alanine transaminase (ALT), body mass index (BMI), serum gamma-glutamyl transferase (GGT), serum triglycerides (TG), serum alkaline phosphatase (ALP), and serum aspartate transaminase (AST) were assessed in both groups.

Results: A significant enhancement (improvement) in BMI, ALT, GGT, ALP, AST, and TG was reported in the exercise group only.

Conclusion: Participation in an 8-week free walking program significantly improves BMI, AST, ALP, ALT, GGT, and TG in children with NAFLD and PKU.

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RESUMEN

Antecedentes: La fenilcetonuria (PKU), un trastorno metabólico autosómico recesivo hereditario, es un trastorno prevalente en los países árabes (1 de cada 6000 bebés se ve afectado por este trastorno) debido a la alta prevalencia de consanguinidad. En niños con PKU, el exceso de peso corporal y sus complicaciones asociadas, como la enfermedad del hígado graso no alcohólico (EHGNA), son muy reportados debido al estilo de vida sedentario, la baja actividad física y la restricción del consumo de las proteínas dietéticas naturales más importantes que pueden representar un riesgo potencial de consumo excesivo de carbohidratos, azúcares y grasas para satisfacer las necesidades energéticas de los niños. Investigar el efecto de un programa de ejercicio de caminata de 8 semanas sobre las enzimas hepáticas en niños con PKU y EHGNA fue el objetivo de este ensayo controlado aleatorizado.
Métodos: Este ensayo clínico sobre la PKU es un ensayo controlado aleatorizado en niños. Se incluyeron cuarenta niños con sobrepeso/obesidad, PKU y EHGNA, de 9 a 12 años de edad. Los niños fueron asignados aleatoriamente a un grupo de ejercicio (n = 20) que recibió un programa de caminata libre de 8 semanas o a un grupo control (grupo en lista de espera, n = 20). Se evaluaron las concentraciones séricas de alanina transaminasa (ALT), índice de masa corporal (IMC), gamma-glutamil transferasa (GGT), triglicéridos (TG), fosfatasa alcalina (FA) y aspartato transaminasa (AST) en ambos grupos.
Resultados: Se informó una mejora significativa del IMC, ALT, GGT, ALP, AST y TG solo en el grupo de ejercicio.
Conclusión: La participación en un programa de caminata libre de 8 semanas mejora significativamente el IMC, AST, ALP, ALT, GGT y TG en niños con EHGNA y PKU.

Introduction

Phenylketonuria (PKU), the inherited metabolic autosomal recessive disorder, is a prevalent disorder in Arabic countries (1 in 6000 babies are affected by this disorder) due to the high prevalence of consanguinity.[1] This metabolic disorder is caused by a deficiency of phenylalanine hydroxylase (PAH), a hepatic enzyme that catalyzes the conversion of phenylalanine (an essential amino acid) into tyrosine.[2]

The classical form of this metabolic inborn error, PKU, is characterized by elevated serum phenylalanine (Phe) level $>1200\,\mu mol/L$. Untreated high levels of Phe are associated with intellectual disability,[3] brain damage, autism, seizures/convulsions, epileptic episodes/attacks, and behavioral/psychiatric disorders.[4]

Restricting dietary protein intake including animal protein sources (such as meat, eggs, milk, or dairy products) and plant protein sources including beans) of PKU, in addition to the prescription of micronutrient-supplemented protein substitutes or dietary formulae is the mainstay of the management of PK.[5]

Because PKU is considered a long-life chronic metabolic problem, besides the increased consumption of carbohydrates and fats, children with PKU may show a low adherence to the recommended intake of Phe-free foods and micronutrient-supplemented protein substitutes or dietary formula (these substitutes may be expensive for low-income families). All these factors not only elevate the levels of serum Phe but are also associated with the development of various cardiovascular risk factors including obesity, dyslipidemia, hypertension, diabetes,[6] metabolic syndrome,[7] and nonalcoholic fatty liver disease[8] (NAFLD, defined as the presence/accumulation of steatosis/fat – mainly triglycerides – in more than 5% of hepatocytes).[9]

Exercise is an essential cornerstone treatment to treat/prevent complications of metabolic disorders,[10–16] especially in NAFLD due to the absence of approved pharmacological therapies.[9] Despite the repeated calls to include PKU patients in a regular exercise program to restrict the development of PKU-related complications,[17] no study assessed the effect of a regular exercise program on liver enzymes in children with PKU-induced NAFLD, so this study aimed to assess this effect.

Materials and methods

Design

In 40 children with PKU, this randomized-controlled exercise trial was designed.

Settings

Posters were installed on the walls of a local children's hospital. Participation in this study was through posters containing appeals to mothers of children with PKU and NAFLD who wish to improve their children's lifestyle through a regular walking program.

Ethics

As ethical aspects, the signature (consent) of the parents of the children participating in the study (Clinical Study ID. NCT06718842), Cairo University's ethical approval (P.T.REC/012/005449), and following the Helsinki guidelines were considered.

Inclusion criteria

Children with classical PKU who were aged from 9 to 12 years old were included. The diagnosis of PKU was performed after a positive newborn screening. Children had been continuously managed with a low-Phe diet since birth.

Children with PKU who were recently diagnosed as NAFLD children were included (the diagnosis of NAFLD was confirmed via abdominal ultrasonography). Also, the clinical/pathological diagnosis of NADFLD in children with PKU was confirmed by elastography-using magnetic resonance imaging. Liver steatosis in all children was calculated/estimated by fatty liver and hepatic steatosis indices.[18]

In this study, the following website: https://www.cdc.gov/healthyweight/bmi/calculator.html was used for the calculation of body mass index (BMI) and the detection of overweight and obesity in children. The following data were entered into the calculator of the above-mentioned: age, height (cm), weight (kg), and sex. Then, automatically the calculator of the website revealed the value of the child's BMI in addition to detecting if this child was underweighted, normal weight, overweight, or obese. Overweight and obese children with PKU and NAFLD were included in this study.

This website detected the BMI of children according to the World Health Organization's growth reference for school-age children.[19]

Exclusion criteria

All included children with PKU and NAFLD were free from other medical diseases such as diabetes mellitus, heart diseases, hypertension, hepatitis, lower-limb orthopedic problems, mental disorders, hormonal/endocrine disorders, respiratory/renal disorders, other genetic disorders, and autoimmune diseases.

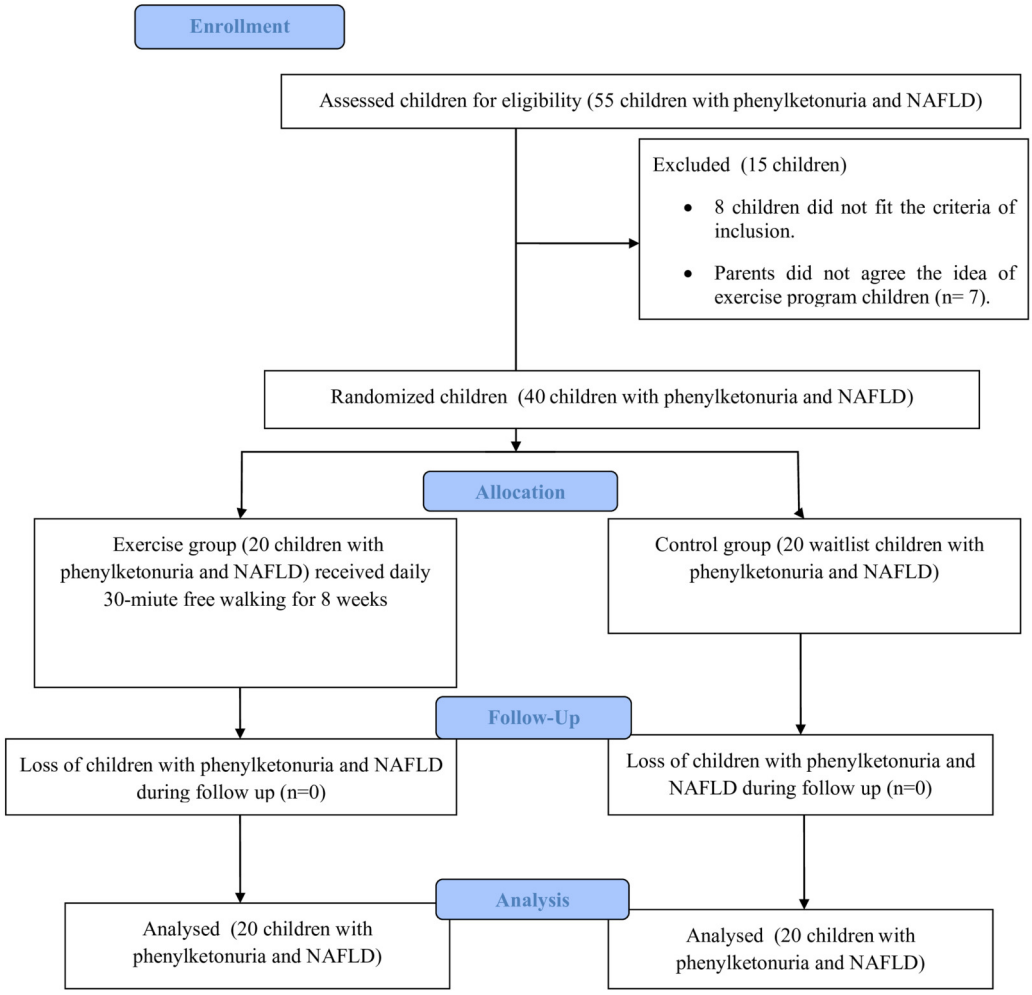

Fig. 1. Flow chart of children with phenylketonuria and NAFLD.

Randomization

From both sexes, 40 children with PKU and NAFLD were randomly assigned – via computer randomization list – into exercise group ($n = 20$) that received an 8-week free walking program or control group (waitlist group, $n = 20$). Both groups were advised to keep the by-physician recommended dietary formula/substitutes and low-Phe natural dietary foods. The randomization (Fig. 1) of children with PKU and NAFLD was done via independent researcher.

Randomization using blocks was used to assign children who satisfied the study's requirements to groups. The independent researcher used a sequentially numbered sealed envelope strategy to disguise allocation. Before beginning the procedure, a nurse opened the envelopes.

Walking program

Children with PKU and NAFLD, together with their parents, were informed of the benefits of programmed walking (30 min daily). The kids were asked or permitted to go freely around the sports club or the closest football field to their house. The day before starting the walking program, children with PKU and NAFLD attended a local sports club for a supervised introductory session of walking training at 60–65% of children's target heart rate (THR). In this session, with the aid of a pulse oximeter, parents were trained to determine and track their children's THR using the Karvonen equation: [(PKU children's heart rate maximum – PKU children's heart rate rest) × (0.60 – 0.65)] + PKU children's heart rate rest].[20]

The day next to the day of the introductory session, the children with PKU and NAFLD were asked or permitted to go/walk freely for 30 min around the sports club or the closest football field to their house. The sessions were conducted at 60–65% of children's THR. Using the online videoconference application (Imo video chat software) that parents of children with NAFLD and PKU had set up on their cell phones, parents and children were kept under observation during the daily designed walking sessions.

Outcomes

The following measurements were done; serum alanine transaminase (ALT, a hepatic enzyme that was assessed as the primary outcome of this PKU trial), BMI, serum gamma-glutamyl transferase (GGT), serum triglycerides (TG), serum alkaline phosphatase (ALP), and serum aspartate transaminase (AST) were assessed.

Blinding

Serum outcomes (ALP, GGT, AST, ALT, and TG) of children of PKU with NAFLD were assessed via an independent assessor (a specialist of medical laboratory analyses who had a diploma in medical analysis) was not informed of the details of the study.

Sample size

This trial's effect size was 1.26 U/L at a power of 95%, with the main/primary outcome being the children's ALT. Sixteen pilot-test

Table 1
Basic data of children with PKU and non-alcoholic fatty liver.

Data	Exercise group ($n = 20$)	Control group ($n = 20$)	P value
Age of phenylketonuria children (years)	10.35 ± 1.13	10.60 ± 1.18	0.497
Body mass index of phenylketonuria children (kg/m^2)	27.94 ± 2.13	29.34 ± 2.73	0.079
Waist circumference (cm) of phenylketonuria children	87.60 ± 7.97	90.90 ± 9.27	0.234
Average phenylalanine (μmol/L)	649.20 ± 119.01	725.50 ± 174.14	0.114
Sex of phenylketonuria children (females:males)	7:13	9:11	0.518
Number of overweight and obese children	4:16	6:14	0.465
Fatty liver index	45.05 ± 4.44	46.95 ± 4.91	0.207
Hepatic steatosis index	44.35 ± 4.68	44.20 ± 3.90	0.913
Controlled attenuation parameter (dB/m)	264.95 ± 28.15	267.40 ± 15.88	0.737
Liver stiffness (kPa)	5.12 ± 0.23	5.13 ± 0.25	0.848
Liver fibrosis (percentage of patients with liver fibrosis)	40	30	

PKU: phenylketonuria; *n*: number. All *P* values are non-significant. Except for sex of children and number of overweight/obese children which were tested via Chi-square test, all data are expressed as mean ± SD.

children with PKU and NAFLD participated in a pilot-test randomized-controlled exercise program, which produced the above-mentioned effect size/magnitude. The G*power sample size program/analysis found that each group required eighteen children with PKU and NAFLD. Two more children with PKU and NAFLD were added to each group to prevent a 10% loss of these children during the implementation of the randomized controlled walking exercise program.

Statistical analysis

To be noted, all data of children with PKU and NAFLD were normally distributed (the Shapiro test confirmed this notice). Besides the pre-treatment sex difference assessed via the Chi-squared test, the pre-interventional statistical differences in PKU children's age, waist circumference, and average phenylalanine between PKU groups were assessed via the unpaired test. Within or between groups of children with PKU and NAFLD, the statistical difference in children's BMI, ALP, AST, GGT, ALT, and TG was assessed via ANOVA (repeated measure). In this randomized-controlled walking exercise trial conducted on 40 children with PKU and NAFLD, the *P* value's significance was < 0.05.

Results

Before starting the program of walking exercise, all basic data (age, Phe, waist circumference, BMI, and sex distribution), as shown in Table 1, or pre-treatment outcomes (BMI, ALT, GGT, ALP, AST, and TG), as shown in Table 2, did not significantly differ between groups.

Regarding the outcomes (BMI, ALT, GGT, ALP, AST, and TG), a significant enhancement (improvement) was reported in the exercise group only after performing a within-group comparison between the pre-and post-values of these outcomes (Table 2).

The performed between-group comparison between the post-values of the outcomes (BMI, ALT, GGT, ALP, AST, and TG) reported a significant enhancement (improvement) in the direction of the exercise group (Table 2).

Discussion

This is the first PKU trial that reports a significant effect of a walking program on liver enzymes (ATT, GGT, AST, and ALP), BMI, and TG in children with PKU and NAFLD. Before this trial, no study discussed the mechanism, effect, and role of exercise in improving liver enzymes in those children.

In accordance with the idea of this study that suggests a presence of NAFLD in children with PKU, a recent study – published in 2023 – reported that the prevalence of NAFLD in children with PKU was higher than that found in sex- and age-matched healthy children. This recent study reported that NAFLD may appear in 26% of children with PKU.[8]

Also, in accordance with the concept of the presence of excess weight among children with PKU, a cross-sectional study conducted on 58 children with PKU reported that half of those children were overweight ($n = 29$) and the rest of them ($n = 29$) had a normal BMI. Moreover, compared to the normal-BMI children with PKU, the development of metabolic syndrome was highly expected in the overweight children with PKU because the overweight children had elevated TG, low high-density lipoprotein, high levels of basal insulin, and high levels of cholesterol.[7] Also, another study reported low levels of high-density lipoprotein in addition to high levels of Phe and TG in children with PKU who had a median age of 10.7 years.[21]

According to a study by Burrage et al.,[22] females with PKU who were classified as non-dietary compliant had a greater prevalence of being overweight; in other words, PKU sufferers who did not follow/track the recommended low-Phe dietary regimen were more likely to be overweight. The low-Phe formula prescribed for PKU sufferers, according to Burrage et al.,[22] may have a role in the lower incidence of being overweight by promoting satiety and reducing the consumption of foods (fats and carbohydrates) high in calories.

Excess weight in children with PKU results from non-adherence to nutritional guidelines of PKU, lack/excess of nutrients,[23] sedentary lifestyle, low physical activity,[24] and restricting the consumption of the most important natural dietary proteins that can pose a potential risk of overconsumption of carbohydrates, sugars, and fats to meet children's energy needs.[8] Excess weight is the main risk factor for the development of cardiovascular risk factors, including central obesity (expressed by an abnormal increase in children's waist circumference), dyslipidemia (elevated levels of TG and low-density lipoprotein in addition to the reduced levels of high-density lipoprotein),[7] and NAFLD.[8]

Exercise is a recommended lifestyle-modification program for the elevated levels of serum liver enzymes. Improved liver enzymes after regular exercise may be justified by the attenuated proliferation of NAFLD patients' hepatic stellate cells, enhanced NAFLD patients' immunity, attenuated production of inflammatory markers, increased synthesis/action of anti-inflammatory biomarkers, and improved resistance of the body against further inflammation/affection of new hepatocytes.[25]

Exercise is a recommended lifestyle modification program[26–30] for elevated levels of serum TG. Regular walking is one type of aerobic exercise that can stimulate lipolysis and accelerate the reduction of visceral fat as well as general body fat. Increased sympathetic and growth hormone activity during these programs can also assist in this process. Exercise has the potential to catabolize TG and TG-rich lipoproteins, enhance TG transport and use within muscles, and improve TG absorption from the bloodstream by increasing the activity of enzymes such as lipoprotein A and lipoprotein lipase.[10,31–34]

Table 2
Outcomes of children with PKU and non-alcoholic fatty liver.

Outcomes	Exercise group (n = 20) Mean ± SD	Control group (n = 20) Mean ± SD	P value (between PKU groups)
Body mass index of phenylketonuria children (kg/m²)			
Before exercise program	27.94 ± 2.13	29.34 ± 2.73	0.079
After exercise program	26.78 ± 2.12	29.41 ± 2.66	0.001*
P value (within-phenylketonuria groups)	< 0.001*	0.312	
Triglycerides (mg/dL) of phenylketonuria children			
Before exercise program	110.35 ± 7.71	116.85 ± 13.38	0.068
After exercise program	101.15 ± 7.19	117.25 ± 14.22	< 0.001*
P value (within-phenylketonuria groups)	< 0.001*	0.498	
Alanine transaminase of phenylketonuria children (U/L)			
Before exercise program	37 ± 7.71	41.40 ± 8.45	0.094
After exercise program	26.85 ± 6.63	41.55 ± 8.32	< 0.001*
P value (within-phenylketonuria groups)	< 0.001*	0.809	
Aspartate transaminase of phenylketonuria children (U/L)			
Before exercise program	26.70 ± 5.47	29.90 ± 5.08	0.063
After exercise program	21.75 ± 4.73	30.15 ± 6.01	< 0.001*
P value (within-phenylketonuria groups)	< 0.001*	0.621	
Gamma-glutamyl transferase (GGT) of phenylketonuria children (U/L)			
Before exercise program	19.30 ± 3.26	21.40 ± 4.14	0.083
After exercise program	15.30 ± 2.34	21.75 ± 4.20	< 0.001*
P value (within-phenylketonuria groups)	< 0.001*	0.327	
Alkaline phosphatase (ALP) of phenylketonuria children (U/L)			
Before exercise program	144.10 ± 15.80	153.70 ± 15.61	0.061
After exercise program	133.25 ± 14.75	154.20 ± 16.08	< 0.001*
P value (within-phenylketonuria groups)	< 0.001*	0.499	

SD: standard deviation; PKU: phenylketonuria; n: number.
* Phenylketonuria children 's P value is significant ($P < 0.05$).

Parallel to the results, in NAFLD adolescents/children with obesity who were aged 12.81 ± 1.02 years and had a BMI equal to 26.68 ± 2.32 kg/m², the regular participation in an interval exercise program significantly improved their TG, ALT, and AST.[35] Also, in NAFLD children aged 10.51 ± 3.18 years, lifestyle modification resulted in a significant enhancement in BMI, AST, ALT, and GGT.[36] Again, 12-week aerobic training is considered a strong weight-management tool for obese children with NAFLD because it can produce a significant improvement in their ALT, AST, ALP, and BMI.[37]

This study is not without some limitations. The reported improvement in BMI, AST, ALP, ALT, GGT, and TG in children with NAFLD and PKU was not tracked as a follow-up measurement, hence covering this limitation in future trials must be managed.

Conclusion

Participation in an 8-week free walking program significantly improves BMI, AST, ALP, ALT, GGT, and TG in children with NAFLD and PKU.

Ethics

As ethical aspects, the signature (consent) of the parents of the children participating in the study (Clinical Study ID. NCT06718842), Cairo University's ethical approval (P.T.REC/012/005449), and following the Helsinki guidelines were considered.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation/writing of this PKU paper, the authors did not utilize AI-generated or AI-assisted programs.

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None declared.

Conflicts of interest

There are no reported conflicts of interests

Data availability

On request.

References

1. Saad K, Elserogy Y, Abdel Rahman AA, et al. ADHD, autism and neuroradiological complications among phenylketonuric children in Upper Egypt. *Acta Neurol Belg*. 2015;115:657–663, http://dx.doi.org/10.1007/s13760-014-0422-8.
2. Burlina A, Leuzzi V, Spada M, Carbone MT, Paci S, Tummolo A. The management of phenylketonuria in adult patients in Italy: a survey of six specialist metabolic centers. *Curr Med Res Opin*. 2021;37:411–421, http://dx.doi.org/10.1080/03007995.2020.1847717.
3. Lichter-Konecki U, Vockley J. Phenylketonuria: current treatments and future developments. *Drugs*. 2019;79:495–500, http://dx.doi.org/10.1007/s40265-019-01079-z.
4. van Spronsen FJ, Blau N, Harding C, Burlina A, Longo N, Bosch AM. Phenylketonuria. *Nat Rev Dis Primers*. 2021;7:36, http://dx.doi.org/10.1038/s41572-021-00267-0.
5. Vardy ERLC, MacDonald A, Ford S, Hofman DL. Phenylketonuria, comorbidity, and ageing: a review. *J Inherit Metab Dis*. 2020;43:167–178, http://dx.doi.org/10.1002/jimd.12186.
6. Azabdaftari A, van der Giet M, Schuchardt M, Hennermann JB, Plöckinger U, Querfeld U. The cardiovascular phenotype of adult patients with phenylketonuria. *Orphanet J Rare Dis*. 2019;14:213, http://dx.doi.org/10.1186/s13023-019-1188-0.
7. Kanufre VC, Soares RD, Alves MR, Aguiar MJ, Starling AL, Norton RC. Metabolic syndrome in children and adolescents with phenylketonuria. *J Pediatr (Rio J)*. 2015;91:98–103, http://dx.doi.org/10.1016/j.jped.2014.06.006.
8. Silveira AM, Lima PL, Alves MRA, et al. Nonalcoholic fatty liver disease in adolescents with phenylketonuria. *J Pediatr (Rio J)*. 2023;99:174–180, http://dx.doi.org/10.1016/j.jped.2022.08.003.

9. Ismail AMA, Saad AE, Draz RS. Effect of low-calorie diet on psoriasis severity index, triglycerides, liver enzymes, and quality of life in psoriatic patients with non-alcoholic fatty liver disease. *Reumatologia*. 2023;61:116–122, http://dx.doi.org/10.5114/reum/162995.
10. Ismail AMA. Metabolic syndrome components response to the conducted 16-week randomised-controlled training trial on an elliptical trainer. *Eur J Physiother*. 2022;25:147–153, http://dx.doi.org/10.1080/21679169.2021.2022756.
11. Ismail AMA. Chat GPT in tailoring individualized lifestyle-modification programs in metabolic syndrome: potentials and difficulties? *Ann Biomed Eng*. 2023;51:2634–2635, http://dx.doi.org/10.1007/s10439-023-03279-x.
12. Ismail AMA. Virtual reality-based exercise in adolescents with polycystic ovarian syndrome-induced fatty liver: an interesting and entertaining method requiring more attention. *Curr Womens Health Rev*. 2025;21, http://dx.doi.org/10.2174/0115734048339094241106052337, e15734048339094.
13. Ali Ismail A, AbdElnabi Mousa N, Mohamed Elgendy S, et al. Effect of lifestyle changes on liver enzymes, triglycerides, sex hormones, and daytime sleepiness in polycystic ovarian syndrome women with obstructive sleep apnea and fatty liver – a randomized controlled trial. *Menopause Rev/Przegląd Menopauzalny*. 2025;24:94–101, http://dx.doi.org/10.5114/pm.2025.152991.
14. Ismail AMA, El-Moatasem AM, El-Moatasem AM. Effect of baduanjin exercise on salivary inflammatory and oxidative markers in the elderly with metabolic syndrome and periodontal disease: a randomized trial. *J Bodyw Mov Ther*. 2025;45:536–544, http://dx.doi.org/10.1016/j.jbmt.2025.09.017.
15. Ismail AMA, Tolba AMN. Effectiveness of lifestyle-modification approach (a randomized-controlled program of diet restriction and treadmill walking exercise) on elderly's metabolic syndrome-associated subjective tinnitus. *Eur Arch Otorhinolaryngol*. 2025;282:4307–4315, http://dx.doi.org/10.1007/s00405-025-09494-7.
16. El-Hadidy H, Ali Ismail AM, El Sayed SG, Ahmed A, Elgohary O. Additive effect of free walking exercise on liver enzymes, fatigue severity, triglycerides, and sleeping quality in obstructive sleep apnea patients with non-alcoholic fatty liver: randomized controlled trial. *Adv Rehabil*. 2025;39:16–27, http://dx.doi.org/10.5114/areh.2025.154202.
17. Ismail AM. ChatGPT-assisted introduction of exercise advice to patients with phenylketonuria: restrictions and advantages. *Health Probl Civiliz*. 2024;18, http://dx.doi.org/10.5114/hpc.2024.140504.
18. Song K, Kwon YJ, Lee E, et al. Optimal cutoffs of fatty liver index and hepatic steatosis index in diagnosing pediatric metabolic dysfunction-associated steatotic liver disease. *Clin Gastroenterol Hepatol*. 2026;24, http://dx.doi.org/10.1016/j.cgh.2025.06.011, 421–431.e6.
19. Dumith SC, Ramires VV, Souza MA, et al. Overweight/obesity and physical fitness among children and adolescents. *J Phys Act Health*. 2010;7:641–648, http://dx.doi.org/10.1123/jpah.7.5.641.
20. Kamal NN, Ragy MM. The effects of exercise on C-reactive protein, insulin, leptin and some cardiometabolic risk factors in Egyptian children with or without metabolic syndrome. *Diabetol Metab Syndr*. 2012;4:27, http://dx.doi.org/10.1186/1758-5996-4-27.
21. de Almeida BNF, Laufer JA, Mezzomo TR, et al. Nutritional and metabolic parameters of children and adolescents with phenylketonuria. *Clin Nutr ESPEN*. 2020;37:44–49, http://dx.doi.org/10.1016/j.clnesp.2020.03.024.
22. Burrage LC, McConnell J, Haesler R, et al. High prevalence of overweight and obesity in females with phenylketonuria. *Mol Genet Metab*. 2012;107(1–2):43–48, http://dx.doi.org/10.1016/j.ymgme.2012.07.006.
23. MacDonald A, Rocha JC, van Rijn M, Feillet F. Nutrition in phenylketonuria. *Mol Genet Metab*. 2011;104:10–18.
24. Sena BDS, Andrade MIS, Silva APFD, Dourado KF, Silva ALF. Overweight and associated factors in children and adolescents with phenylketonuria: a systematic review. *Rev Paul Pediatr*. 2020;38, http://dx.doi.org/10.1590/1984-0462/2020/38/2018201, e2018201.
25. Ismail AMA, Gressy NSSAE, Hegazy MD, Abdel-Halim Elfahl AM, Ahmed OSM. Randomized controlled effect of treadmill walking exercise on liver enzymes, psychological burden, and erectile dysfunction in men with hepatitis C. *Prz Gastroenterol*. 2024;19:263–270, http://dx.doi.org/10.5114/pg.2023.130334.
26. Ismail AM, Gadallah NG, Elfahl AM. Apnea-hypopnea index, blood pressure, daytime sleepiness, and sleeping quality in obstructive sleep apnea: randomized-controlled responses to Shitali respiratory training. *Respir Med*. 2025;252:108608, http://dx.doi.org/10.1016/j.rmed.2025.108608.
27. Yasin FB, Abdulla FA, Madhanagopal J, Shallan A, Sheeha BB, Ismail AMA. New flexi force sensor integrated seat pan device with real-time biofeedback for instant poor posture alert among office workers: a pilot study. *Ir J Med Sci*. 2025;194:2225–2232, http://dx.doi.org/10.1007/s11845-025-04104-1.
28. Ismail AMA. Exercise for post-COVID female sexual dysfunction. *Curr Womens Health Rev*. 2024;20, http://dx.doi.org/10.2174/1573404820666230602143426, e020623217610.
29. Youssef Mohamed SM, Shehata Kelini KI, Mahmoud Ahmed SS, et al. Effect of pranayama versus aerobic exercise on hematological parameters in women with iron-deficiency anemia. *SPORT TK-EuroAmerican J Sport Sci*. 2025;14:155, http://dx.doi.org/10.6018/sportk.694821.
30. Ismail AMA, Yusof MR, Khairul-Asri MG, Ahmad Faiz NMG, Zakaria MZ, Ashraf M. Maintaining good sexual health in men with cardiovascular risk factors: ChatGPT may be a good lifestyle-modification advising friend. *Androl Genital Surg*. 2024;25:63–64, http://dx.doi.org/10.62968/2070-9781-2024-25-1-63-64.
31. Ismail A, Sallam S, Salem I, et al. Liver enzymes in non-alcoholic fatty liver diseases: response to pyram idal versus continuous aerobic training. *Russian Arch Inter Med*. 2025;15:415–425, http://dx.doi.org/10.20514/2226-6704-2025-15-6-415-425 [in Russian].
32. Ismail AMA. Obstructive sleep apnea: it is time to focus on performing aerobic exercise that may improve erectile dysfunction associated with the disease. *J Sex Ment Health*. 2026;24, http://dx.doi.org/10.5603/jsmh.105426, e03326001.
33. Mohamed AMA, Ismail AMA, Ali RR, et al. Efficacy of baduanjin exercise in patients with idiopathic chronic fatigue who additionally survived from COVID-19 contraction: a randomized controlled trial. *Int J Human Move Sports Sci*. 2025;13:708–718, http://dx.doi.org/10.13189/saj.2025.130406.
34. Ali Ismail AM. Is there an effect of lifestyle changes (exercise and diet control) on the suggested connection between dry eye syndrome and psoriasis? *Health Probl Civiliz*. 2025;19:247–248, http://dx.doi.org/10.5114/hpc.2024.140002.
35. Iraji H, Minasian V, Kelishadi R. Changes in liver enzymes and metabolic profile in adolescents with fatty liver following exercise interventions. *Pediatr Gastroenterol Hepatol Nutr*. 2021;24:54–64, http://dx.doi.org/10.5223/pghn.2021.24.1.54.
36. Pawel M, Anna M, Katarzyna M, Wojciech S, Magdalena F. A decline in aminotransferase activity due to lifestyle modification in children with NAFLD. *J Pediatr Res*. 2021;8:41–48, http://dx.doi.org/10.4274/jpr.galenos.2020.26042.
37. Zinvand Lorestani A, Rahmati M, Mirnasuri R. Effect of 12 weeks of aerobic training on liver enzymes, thyroid hormones, and anthropometric indices of obese children. *Zahedan J Res Med Sci*. 2020;22, http://dx.doi.org/10.5812/zjrms.88821, e88821.