Physical Activity and Hormones (J Physic Act Horm)
Vol. 6 Autumn 2025

The Effect of Resistance-Endurance Training on Anxiety, Depression, and Levels of Testosterone and Cortisol Hormones During the Maintenance Chemotherapy Phase in Children with Acute Lymphoblastic Leukemia

Mastaneh Taati Moghadam Ziyabari[1]
Department of Physical Education and Sport Sciences, Ra.C., Islamic Azad University, Rasht, Iran

Bahram Darbandi[2]
Associate Professor, Pediatric Hematologist-Oncologist, Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran

Adel BagherSalimi[3]
Associate Professor, Pediatric Hematologist-Oncologist, Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran

Mercedeh Enshaei[4]
Assistant Professor, Pediatric Hematologist-Oncologist, Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran

Mohadeseh Dadmanesh[5]
Department of Physical Education and Sport Sciences, Ra.C., Islamic Azad University, Rasht, Iran

Anis Salimi[6]
Department of Physical Education and Sport Sciences, Ra.C., Islamic Azad University, Rasht, Iran

ABSTRACT

Introduction: The aim of this study was to investigate the effect of resistance-endurance training (RET) on anxiety, depression, and the ratio of testosterone and cortisol hormones in children with acute lymphoblastic leukemia (ALL) during the maintenance chemotherapy phase.

Material & Methods: This clinical trial study was design with pre and post-test. The statistical population included children with ALL referred to 17th Shahrivar education, research & remedial center Hospital in Rasht city during the maintenance chemotherapy period. From these patients, 30 volunteer children were selected and randomly divided into control (CG, n=15) and experimental group (EG, n=10). Testosterone and cortisol levels were determined using blood samples test, and anxiety and depression were obtained the Spence Children's Anxiety Scale (1997) and the Children's Depression Inventory (Kovacs, 1992) questionnaires, respectively. The EG performed RET for 12 weeks (three 45-minute sessions per week) under the supervision of a trainer at Hospital, and other days, both groups were asked to perform at least twice a week, 30 minutes of walking or cycling with stretching exercises daily. Data were analyzed using ANCOVA and paired t-test in SPSS software version 27.

Results: The results showed that resistance-endurance exercises have a significant effect on reducing anxiety and depression ($p < 0.05$), but there is no significant effect on the testosterone to cortisol ratio ($p > 0.05$).

Conclusion: RET can be considered as an effective complementary intervention to improve the psychological and physical aspects of children with ALL.

Keywords: Anxiety, Depression, Testosterone, Exercises, Cortisol, Acute Lymphoblastic Leukemia.

***Correspondence:** dadmaneshmohadeseh@gmail.com
Received: Oct 2025; **Revised:** Nov 2025; **Accepted:** Dec 2025.
DOI: https://doi.org/10.71878/jpah.2025.1222560

1. Introduction

ALL is the most common type of cancer in children, with approximately 60% of cases occurring in individuals under 20 years of age (1). This disease, due to its aggressive nature, requires complex treatment protocols that include three main phases: induction of remission, consolidation, and maintenance. The maintenance phase encompasses the longest treatment period (2 to 3 years) and its primary goal is to prevent disease relapse (2). In this phase, children have more suitable conditions for non-pharmacological interventions owing to relative clinical stability. However, side effects of chemotherapy drugs such as vincristine and dexamethasone, including musculoskeletal and neurological disorders, pose significant challenges to the physical and mental health of children (3). Recent studies indicate that more than 30% of children with ALL experience symptoms of anxiety and depression during treatment, which are associated with high levels of cortisol (stress hormone) and disruption in testosterone balance (4).

Anxiety and depression in children with ALL often arise from a combination of psychological factors (such as fear of disease relapse) and biological factors (such as the cytotoxic effects of chemotherapy), which are exacerbated by increased cortisol levels (5). Recent research emphasizes the role of stress hormones in this process; for example, high cortisol levels can disrupt the hypothalamic-pituitary-adrenal (HPA) axis and lead to treatment-resistant depression. Concurrently, reduced testosterone in these patients, which often occurs due to suppression of the gonads by drugs, is associated with chronic fatigue and decreased motivation (6). These hormonal changes not only affect mental health but can also impact physical growth and immune function in children. Understanding these mechanisms provides a foundation for targeted interventions, where hormonal regulation can serve as a bridge between physical and mental health.

RET, as a non-pharmacological intervention, have shown high potential for modulating anxiety, depression, and hormonal levels in children with cancer (7). RET have high potential for improving mental and physical health due to their ability to increase endorphin and serotonin secretion, reduce systemic inflammation, and regulate the HPA axis (8). These exercises can also help strengthen muscles, reduce fatigue, and improve self-confidence by increasing testosterone, which is highly valuable for children undergoing heavy chemotherapy treatments (9). Studies including meta-analyses on healthy children and patients, indicate that the combination of RET can reduce cortisol levels and increase testosterone without causing significant side effects (10). In the context of childhood cancer, similar interventions in adults have led to a 20–30% improvement in depression symptoms, and preliminary evidence in children with ALL indicates reduced anxiety through increased endorphins and regulation of the HPA axis. These exercises also have a positive impact on the immune system and reduce systemic inflammation, which can contribute to an overall improvement in quality of life.

Despite emerging evidence, exercise interventions, particularly RET, can be effective in reducing fatigue and depression symptoms in cancer patients (1, 11). However, most of these studies have focused on adults, and there is limited data on the effects of these exercises on children with ALL, especially during the maintenance chemotherapy phase. This study, by filling the existing research gap, takes an important step towards improving treatment outcomes and quality of life for children with ALL. Given the increasing prevalence of childhood cancer and the negative impacts of chemotherapy treatments, the need for effective non-pharmacological interventions is felt more than ever. Examining the effect of RET on anxiety, depression, and levels of testosterone and cortisol hormones can provide a basis for designing more comprehensive treatment programs that pay attention not only to physical aspects but also to mental health, quality of life of patients and their families. This research can serve as an initial model for future studies in this field and pave the way for improving supportive care in children with cancer.

2. Methodology

2.1. Materials and methods

The present study was applied in terms of purpose and clinical trial in methodology, adopting a pre and post-test approach with two Control (CG) and Experimental Group (EG), as the necessary measurements were taken from the participants before implementing the exercise protocol, and measurements were repeated after its implementation. It is noteworthy that prior to implementing the protocols, an ethics code numbered (IR.IAU.RASHT.REC.1402.065) was obtained.

2.2. Participants

The statistical population of this study consisted of children with ALL referred to 17th Shahrivar Hospital in Rasht who were undergoing the maintenance chemotherapy phase. After applying inclusion and exclusion criteria contain: age range of 5 to 12 years; having stable physical conditions for participating in the exercise; participants without medical issues such as structural heart abnormalities, relapse of ALL symptoms, or clinical heart failure symptoms; children were included in the study based on the treating physician's approval; children who had been in this treatment phase for more than one month; lack of consent to participate in the present study;

children taking medications that restrict physical activity or medications that could affect the results of the present study were excluded from this clinical trial; children with more than two weeks of absence from the research exercise were withdrawn from the study. 30 volunteer patients were randomly divided into two equal group. Ultimately, 5 participants from the experimental group withdrew from the present study, as due to hospitalization or their condition being unsuitable to continue participating in the training program.

2.3. Measurements

In the first stage, the patients' weight (kg) and height (cm) were measured using an electronic height and weight scale (SECA model 769; Made in Germany; Accuracy of 0.1 kg and 0.1 cm). Subsequently, questionnaires (Spence Children's Anxiety Scale – Parent form (1999) (12); Children's Depression Inventory (CDI)(13)) were administered to the patient’s parents as pre and post-tests.

Blood sampling was performed in the 8 AM of the vascular measurement after a 12-h overnight fast, to measure plasma hormones. After centrifuge of blood sample at 3500 rpm for 3 minutes (model 3500BT, biotechnical centrifuge, Italy), the serum samples were stored at -70°C. ELISA reader (3200DANA and ELISA washer 2600DANA, Garni Riz Pardaz Co; Iran), and testosterone and cortisol assay kit (Beta Biomed Co., Netherlands) for hormonals analysis were used (sensitivity 0.083 ng/mL and 1.6 ng/mL, respectively).

2.4. Intervention

Exercise Protocol: The exercises were conducted under the supervision of sports trainers at 17th Shahrivar Hospital in Rasht, three sessions per week. To maintain activity on the other days of the week, parents of the children were asked to ensure that both groups engaged in physical activity at least twice a week, including: (30 minutes of walking or cycling, performing stretching exercises, and balance exercises (walking on an imaginary line with eyes open and closed)) (14-16). They were required to report the performed activities in the social media group formed and share relevant photos with the trainers of this research. In addition, parents were asked to supervise the exercises. The duration, number, and intensity of the exercise in the present study are detailed in Table 1.

Table 1. *Exercise Protocol (14)*

Week	Duration of Exercise (minutes)	Number of Movements	Number of Sets	Work-to-Rest Ratio	Work Time (seconds)	Rest Time (seconds)	Rest Between Sets (seconds)	Exercise Intensity (percentage)
1-3	20	10	3	1:1	10	10	60	40 to 50
4-6	23	10	3	1:1	15	10	60	50 to 60
7-9	28	10	3	2:1	20	15	60	60 to 70
10-12	35	10	3	1:1	25	25	60	70 to 75

In the present study, three exercise methods (yoga, aerobic exercise, and resistance training) were used, as described in Table 2.

Table 2. *Yoga Exercise Protocol*

Week	Yoga Exercises **(16)**
1-3	Proper standing or mountain - tree (modified) - chair - standing forward bend - airplane - gorilla - rag doll - floating tree - lunge
4-6	Warrior 1 - warrior 2 - child's pose - easy pose - airplane - tree - cobra pose - bow pose - cat-cow
7-9	Plank - side plank - half camel pose - bird dog - table pose - child's pose - downward dog - low lunge - spinal twist - hero pose
10-12	Camel pose - boat - bridge - frog - dancer - locust - plank - cobra - bow - bird dog
Week	Aerobic Exercises (15)
1-3	Marching in place - V step - high knees - butt kicks - front kicks - side kicks - jumping jacks - rope jumping - lunge - side-to-side jumps
4-6	Hopscotch - jumping squat - high knees - speed marching in place - jumping jacks - rope jumping - star jumps - V step - cross step - side kicks
7-9	Hopscotch - V step - high knees - butt kicks - front kicks - side kicks - jumping jacks - rope jumping - lunge - side-to-side jumps
10-12	Burpees - jumping squat - high knees - jumping jacks - rope jumping - side kicks - mambo cha-cha - front kicks - side kicks - side-to-side jumps
Week	Resistance Exercises (14)
1-3	Heel raises - single-leg toe stand - mini squat with wall support - raising and lowering hoop - squat - step-ups - side squat - forward walking - walking on a line - balance with ball
4-6	Heel raises - windmill - mini squat with wall support - raising and lowering hoop - squat - step-ups - side squat - forward walking - walking on a line - balance with ball
7-9	Heel raises - single-leg toe stand - mini squat with wall support - raising and lowering hoop - squat - step-ups - side squat - forward walking - walking on a line - balance with ball
10-12	High jumping - bicep curl - mini squat with wall support - jump and switch - squat - step-ups - side squat - forward walking - walking on a line - balance with ball

2.5. Statistical Methods

In this study, both descriptive and inferential statistics were employed. Descriptive statistics were used to describe the findings in the form of tables and charts, presenting means and standard deviations. For inferential statistics, given the normal distribution of the data (Shapiro-Wilk test), paired t-tests and ANCOVA (one-way analysis of variance with the pre-test as a covariate) were applied. The significance level was set at 0.05, and all these analyses were conducted using SPSS software (IBM Corporation; Version 27); furthermore, the figures were created using GraphPad Prism (GraphPad Software, Inc; Version 10).

3. Results

The values of the research variables are presented in Table 3.

Table 3. *Values of the Research Variables in CG and EG Groups*

Components		EG (n=10)	CG (n=15)
		Mean ± Standard Deviation	Mean ± Standard Deviation
Age (years)		8.95 ± 2.98	7 ± 4.74
Height (cm)		129.42 ± 14.58	113 ± 5.66
Weight (kg)		29 ± 12.21	19.95 ± 2.05
Anxiety	Pre-test	76.85 ± 8.37	79.50 ± 1.29
	Post-test	47.57 ± 7.80	84.75 ± 2.22
Depression	Pre-test	14.71 ± 2.99	17.50 ± 1.29
	Post-test	9.78 ± 2.08	18 ± 0.82
Testosterone (ng/dL)	Pre-test	0. 015 ± 0.02	0.015 ± 0.017
	Post-test	0.031 ± 0.04	0.015 ± 0.016
Cortisol (ng/dL)	Pre-test	61.14 ± 17.50	66 ± 22.73
	Post-test	59.35 ± 17.61	66 ± 23.37
Testosterone to Cortisol Ratio (ng/dL)	Pre-test	0.25 ± 0.37	0.00022 ± 0.00019
	Post-test	0.55 ± 0.72	0.00022 ± 0.00019

CG: Control Group; EG: Experimental Group

Table 4. *Correlated t-statistics of variables*

Variable	Group	Mean Difference ± Standard Deviation	t-statistic	Significance
Anxiety	Experimental	7.77 ± 29.28	14.103	0.001*
	Control	-3.095 ± 5.25	-3.392	0.043*
Depression	Experimental	1.730 ± 4.928	10.657	0.001*
	Control	0.577 ± -0.500	-1.732	0.182
Testosterone to Cortisol Ratio (ng/dL)	Experimental	0.00066 ± -0.000301	-1.695	0.114
	Control	0.00019 ± 0.00022	-1.315	0.109

The results of (Table 4) the paired t-test indicated a statistically significant difference between the pre- and post-test anxiety scores in the experimental group ($p<0.05$), denoting a significant decrease in anxiety at post-test. The paired t-test results also showed a statistically significant difference between the pre- and post-test anxiety scores in the control group ($p<0.05$), indicating a significant increase in anxiety at post-test. A statistically significant difference was found between the pre- and post-test depression scores in the experimental group ($p<0.05$), reflecting a significant decrease in depression at post-test. The results of the paired t-test showed no statistically significant difference between the pre- and post-test depression scores in the control group ($p>0.05$). No statistically significant difference was found between the pre- and post-test values for the testosterone to cortisol ratio in either the experimental or the control group ($p>0.05$).

To test the hypotheses, ANCOVA with the pre-test as a covariate was performed, as shown in Table 5.

Table 5. *ANCOVA Results for Anxiety, Depression, and Testosterone to Cortisol Ratio*

Variables		Sum of Squares	Degrees of Freedom	Mean Square	Statistic	Significance	Eta Squared
Anxiety	Between Groups	4525.801	2	2262.900	58.453	0.001*	0.886
	Pre-test	111.169	1	111.169	2.872	0.111	0.161
Depression	Between Groups	250.296	2	125.148	104.395	0.001*	0.933
	Pre-test	9.666	1	9.666	8.063	0.012*	0.350
Testosterone to Cortisol Ratio (ng/dL)	Between Groups	1.494	2	7.468	1.978	0.173	0.209
	Pre-test	0.000	1	0.000	0.000	1	0.000

*: $p < 0.05$

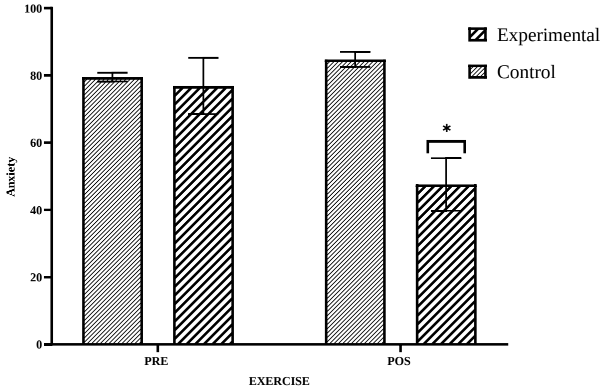
The results in the above table indicate that there is a significant difference between the two groups in anxiety and depression ($p < 0.05$), but no significant difference in the testosterone to cortisol ratio ($p > 0.05$). Table 5 presents the results of the Bonferroni post-hoc test.

Table 6. *Bonferroni Post-Hoc Test for Anxiety and Depression*

Component	Groups	Mean Difference	Standard Error	Significance Level
Anxiety	EG vs. CG	-35.868	3.569	0.001*
Depression	EG vs. CG	-6.611	0.679	0.001*

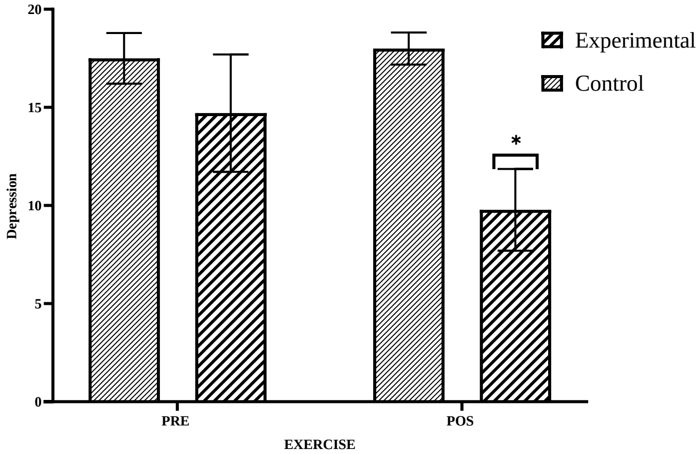
CG: Control Group; **EG:** Experimental Group
*: $p < 0.05$

Based on the results obtained from the Bonferroni test, anxiety and depression in the experimental group showed a significant decrease compared to the control group after resistance-endurance training ($p < 0.05$). Figures 1 to 3 illustrate the changes in anxiety values.



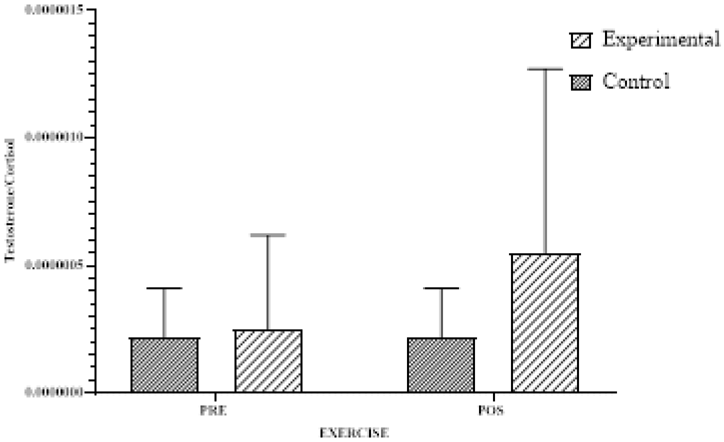
*: p<0.05

Figure 1. The Effect of RET on Anxiety in Children with ALL during the Maintenance Group Phase



*: p<0.05

Figure 2. The Effect of RET on Depression in Children with ALL during the Maintenance Group Phase



*: p<0.05

Figure 3. The Effect of RET on the Testosterone to Cortisol Hormone Ratio in Children with ALL during the Maintenance Group Phase

4. Discussion

Findings revealed that resistance-endurance training has a significant effect on reducing anxiety in children with acute lymphoblastic leukemia during the maintenance phase. In this regard, Meyer and Herring (5) in their systematic review demonstrated that resistance training can reduce anxiety through regulation of the hypothalamic-pituitary-adrenal (HPA) axis, which is consistent with the present finding. Furthermore, Coombs et al. (4) reported that combined exercise interventions in children with acute lymphoblastic leukemia led to a 25% reduction in anxiety, which aligns with the reduction observed in this study. However, the study by Ebadi Nejad et al. (17), which only noted a reduction in anxiety through aerobic exercise and did not investigate the effects of resistance training, is not entirely consistent with the present finding, although its overall results support the hypothesis.

The significant reduction in anxiety in children with acute lymphoblastic leukemia may be linked to increased secretion of endorphins and serotonin. These neurotransmitters function by inducing a sense of calm and reducing the body's stress responses. Resistance-endurance training stimulates the central nervous system, increases the production of these substances, and can modulate the hyperactivity of the hypothalamic-pituitary-adrenal axis, which is elevated in children undergoing chemotherapy due to chronic stress (5). This mechanism is particularly effective in children with acute lymphoblastic leukemia, as chemotherapy agents such as vincristine and dexamethasone can increase cortisol levels and exacerbate anxiety, whereas regular exercise breaks this cycle by reducing stress-related inflammatory responses. Another key mechanism is the reduction of plasma cortisol levels through the regulation of glucocorticoid receptors. Resistance-endurance training, by creating controlled stress, reduces the body's sensitivity to cortisol, thereby diminishing anxiety responses (4). In children with acute lymphoblastic leukemia, where chemotherapy causes chronic elevation of cortisol, this reduction can help improve HPA axis function and alleviate anxiety symptoms by reducing neuroinflammation. Increased blood flow and oxygenation to the brain, particularly in regions such as the hippocampus and amygdala, is another mechanism that reduces anxiety. Resistance-endurance training, by improving cardiopulmonary capacity, remodels neural networks associated with fear and anxiety (18). In children with acute lymphoblastic leukemia who face cognitive impairments due to prolonged hospitalization and treatment side effects, this mechanism may help reduce anxiety related to fear of disease relapse. Reducing systemic inflammation by lowering levels of inflammatory cytokines such as IL-6 and TNF-α is another mechanism influencing anxiety (11). Resistance-endurance training reduces chronic inflammation caused by chemotherapy by increasing the body's antioxidant capacity, thereby inhibiting inflammatory pathways associated with anxiety. This effect in children with acute lymphoblastic leukemia, whose immune systems are compromised, could help reduce anxiety stemming from infections or side effects.

The obtained finding indicated that resistance-endurance training has a significant effect on reducing depression in children with acute lymphoblastic leukemia ($p< 0.05$). This aligns with the finding of Masoud et al. (11), who reported that exergaming in children with acute lymphoblastic leukemia led to a 15% reduction in depression, which is consistent with the present finding and indicates the potential of exercise interventions for improving psychological symptoms. Additionally, Gordon et al. (7) reported a 30% reduction in depression with resistance training in adults, which could be generalized to children. However, the study by Hosseini et al. (19), which focused on working children and reported the effect of exercise on depression without investigating acute lymphoblastic leukemia, is not directly aligned with our finding, although its overall results confirmed a reduction in depression.

From a physiological perspective, the reduction in depression may be related to increased serotonin and dopamine. These neurotransmitters function by improving mood and reducing depressive symptoms (7). Resistance-endurance training stimulates the brain's reward system, increases the production of these substances, and can break the cycle of depression in children with acute lymphoblastic leukemia who face reduced motivation due to long-term treatments. This effect is particularly associated with a reduction in general fatigue, a primary factor in depression among these patients. Another key mechanism may be the increase in BDNF (a crucial protein found in the brain and spinal cord that aids the growth, survival, and function of nerve cells [neurons]) in the hippocampus, which enhances neuroplasticity (the brain's ability to change and adapt throughout an individual's life). Resistance-endurance training improves cerebral blood flow, increases BDNF, and regenerates neural networks damaged by chemotherapy stress (5). In children with acute lymphoblastic leukemia, this mechanism could help reduce depression arising from cognitive impairments, as BDNF plays a protective role against drug-induced cellular apoptosis. Furthermore, increased endorphins, as natural analgesics, can enhance feelings of happiness and reduce depression. Resistance training, by creating controlled muscular stress, stimulates endorphin release (11); in children with acute lymphoblastic leukemia who face pain and fatigue, this effect can help improve mood. This mechanism is accompanied by a reduction in physical symptoms of depression, such as lack of energy. Resistance-endurance training reduces chronic chemotherapy-induced inflammation by increasing antioxidant capacity, thereby alleviating depression associated with neuroinflammation (10). This effect in children with acute lymphoblastic leukemia, whose immune systems are affected, could help reduce depression related to infections. Improved muscle strength and physical function can increase self-confidence and reduce depression. Resistance training strengthens anabolic pathways, reducing feelings of incapacity (6); in children with acute lymphoblastic leukemia who become depressed due to muscle weakness, this mechanism could have a protective role.

Findings revealed that resistance-endurance training does not have a significant effect on the testosterone-to-cortisol ratio in children with acute lymphoblastic leukemia ($p>0.05$). Zeng et al. (10) reported an increased testosterone-to-cortisol ratio associated with reduced anxiety, which conflicts with the non-significant change in the present study and may be related to population differences (non-cancer university students versus children with acute lymphoblastic leukemia). Waddington et al. (9) showed increased testosterone with resistance training, but in conditions without chemotherapy, whereas in this study, the effects of chemotherapy may have neutralized this change. The study by Paahoo et al. (20) also reported no significant effect on testosterone, which aligns with the present finding.

From a physiological perspective, the non-significant effect on the testosterone-to-cortisol ratio may be due to suppression of the hypothalamic-pituitary-gonadal axis by chemotherapy. Drugs such as dexamethasone inhibit testosterone production, and even the stimulus from resistance-endurance training cannot compensate for this suppression. This mechanism in children with acute lymphoblastic leukemia, whose gonads are affected (9), could explain the lack of significant change. Another mechanism is the limited response of the HPA axis to exercise under chronic stress. Chemotherapy increases cortisol, and exercise may be unable to reduce this level due to insufficient intensity. This catabolic imbalance stabilizes the testosterone-to-cortisol ratio, and in children with acute lymphoblastic leukemia with chronic inflammation, this effect is prominent (5). The intervention timing may have been insufficient for increasing testosterone; resistance training typically increases testosterone after more than 12 weeks (6), but if the duration is shorter, this effect is limited. In children with acute lymphoblastic leukemia whose bodies are under treatment pressure, this delay could be the reason for the non-significant change. Malnutrition or chemotherapy side effects reduce anabolic capacity. This condition disrupts anabolic pathways and shifts the testosterone-to-cortisol ratio towards catabolism (11). In children with acute lymphoblastic leukemia with reduced appetite, this mechanism could explain the results. Systemic inflammation, with increased cytokines, inhibits the hormonal response. Resistance-endurance training under conditions of high inflammation cannot increase testosterone and alter the testosterone-to-cortisol ratio (10). This effect is prominent in children with acute lymphoblastic leukemia undergoing chemotherapy. Finally, individual differences such as age, gender, or drug dosage increase response variability. This heterogeneity could be the reason for failing to achieve a significant change in the testosterone-to-cortisol ratio, particularly in a sample of children with acute lymphoblastic leukemia whose clinical conditions are diverse.

It should be noted that this study had limitations, including (age range; consumption of drugs such as "vincristine", "prednisolone", and "intrathecal methotrexate" during the maintenance treatment phase; level of physical activity at home; participants' sleep duration; type of diet; participants' psychological condition; genetic and hereditary characteristics). It is also suggested that studies be designed to investigate the effects of supervised exercise training compared to unsupervised (home-based) training. These studies could involve more in-depth assessments of the type, intensity, and dosage of exercises. Furthermore, it is recommended that a combined, long-term, moderate-intensity intervention programme, comprising supervised resistance and endurance training, be designed and implemented in hospitals affiliated with Iran University of Medical Sciences. This programme could be optimized in collaboration with the pediatric oncology department, using psychological assessment tools (such as anxiety and depression questionnaires) and hormonal assays (testosterone and cortisol) pre- and post-intervention, so that hormonal effects also become notable. The results of this study could serve as local evidence for integrating exercise into standard treatment protocols and improving the quality of life for these patients.

5. Conclusion

Based on the conducted examination, it can be inferred that RET leads to a reduction in anxiety and depression in children with ALL during the maintenance chemotherapy phase ($p < 0.05$); however, RET does not have a significant effect on the testosterone to cortisol hormone ratio in the experimental group of children with ALL during the maintenance chemotherapy phase ($p > 0.05$). Accordingly, RET may have improving effects on the psychological and physical factors of children with acute lymphoblastic Leukemia. It is recommended to design and implement a combined and long-term intervention with moderate intensity, including resistance and endurance exercises under the supervision of sports physiology specialists, in hospitals affiliated with Iran University of Medical Sciences. This RET can be optimized through collaboration with the pediatric oncology department and the use of psychological assessment tools (such as anxiety and depression questionnaires) and hormonal tests (testosterone and cortisol) before and after the intervention, to make hormonal effects noticeable; the results of this study can serve as local evidence for integrating exercise into standard treatment protocols and improving the quality of life for these patients.

6. Acknowledgment

We hereby express our sincere gratitude and appreciation to the esteemed physicians of the oncology department at 17th Shahrivar Hospital in Rasht, who assisted us in realizing this research through their valuable guidance and support. We also sincerely thank the dear children in the ALL department and their respected parents, who played an effective role in advancing this study through their sincere and unconditional cooperation.

Conflict of interests: The authors declare that they have no conflict of interest relating to the publication of this manuscript.

References

1. Zhang B, Jin X, Kuang X, Shen B, Qiu D, Peng J, et al. Effects of a Virtual Reality-Based Meditation Intervention on Anxiety and Depression Among Patients With Acute Leukemia During Induction Chemotherapy: A Randomized Controlled Trial. Cancer Nurs. 2023;47(3):E159-E67. DOI: 10.1097/NCC.0000000000001196
2. Özbay İ, Kabak VY, Uysal SA. Effect of virtual exercise program on depression level and family's perception during COVID-19 pandemic in child cancer survivor: a case report. Journal of Exercise Therapy and Rehabilitation. 2024;11(1):63-8. DOI: 10.15437/jetr.1277468
3. Rijckmans E, Bordon V, de Ravel T, Baert E, Jansen AC, Stouffs K. Macrocephaly? Do not forget SUFU. Pediatric Neurology. 2024;151:34-6. DOI: 10.1016/j.pediatrneurol.2023.12.010
4. Coombs A, Schilperoort H, Sargent B. The effect of exercise and motor interventions on physical activity and motor outcomes during and after medical intervention for children and adolescents with acute lymphoblastic leukemia: A systematic review. Critical reviews in oncology/hematology. 2020;152:103004. DOI: 10.1016/j.critrevonc.2020.103004
5. Herring MP, Meyer JD. Resistance exercise for anxiety and depression: efficacy and plausible mechanisms. Trends in molecular medicine. 2024;30(3):204-6. DOI: 10.1016/j.molmed.2024.01.005
6. Hayta U, Dinc N, Taneli F. Effects of 8-week strength training on basal hormone levels, sex hormone binding globulin, insulin-like growth factor binding protein-3, oxidative stress markers, and IL-6 levels in adolescent athletes. Hormones. 2025;24(1):15-22. DOI: 10.1007/s42000-025-00627-5
7. O'Sullivan D, Gordon BR, Lyons M, Meyer JD, Herring MP. Effects of resistance exercise training on depressive symptoms among young adults: A randomized controlled trial. Psychiatry research. 2023;326:115322. DOI: 10.1016/j.psychres.2023.115322
8. Hooke MC, Mathiason MA, Blommer A, Hutter J, Mitby P, Taylor O, et al. Symptom clusters, physical activity, and quality of life: a latent class analysis of children during maintenance therapy for leukemia. Cancer nursing. 2022;45(2):113-9. DOI: 10.1097/NCC.0000000000000982
9. Waddington F, Amerikanou M, Brett J, Watson E, Abbots V, Dawson P, et al. A systematic review to explore the effectiveness of physical health and psychosocial interventions on anxiety, depression and quality of life in people living with blood cancer. Journal of psychosocial oncology. 2024;42(1):113-47. DOI: 10.1080/07347332.2023.2267610
10. Zeng Q, Zhang Y, Li H, Yuan J, Feng D, Zhu G. The effects of a 12-week moderate-intensity continuous training intervention on depression, anxiety, and stress in sedentary female college students: a focus on negative emotion regulation. Frontiers in Psychology. 2025;16:1507198. DOI: 10.3389/fpsyg.2025.1507198
11. Masoud AE, Shaheen AAM, Algabbani MF, AlEisa E, AlKofide A. Effectiveness of exergaming in reducing cancer-related fatigue among children with acute lymphoblastic leukemia: a randomized controlled trial. Annals of medicine. 2023;55(1):2224048. DOI: 10.1080/07853890.2023.2224048
12. Spence SH. Structure of anxiety symptoms among children: a confirmatory factor-analytic study. Journal of abnormal psychology. 1997;106(2):280.
13. Kovacs M, Staff M, Kovács M. Children's Depression Inventory 2 (CDI2): Multi-Health Systems (MHS); 2010.
14. Lambert G, Alos N, Bernier P, Laverdière C, Drummond K, Dahan-Oliel N, et al. Patient and parent experiences with group telerehabilitation for child survivors of acute lymphoblastic leukemia. International Journal of Environmental Research and Public Health. 2021;18(7):3610. DOI: 10.3390/ijerph18073610
15. Abd El Baky AM, Elhakk SMA. Impact of aerobic exercise on physical fitness and fatigue in children with acute lymphoblastic leukemia. International Journal of Therapies and Rehabilitation Research. 2017;6(2):137. DOI: 10.5455/ijtrr.000000245
16. Diorio C, Schechter T, Lee M, O'Sullivan C, Hesser T, Tomlinson D, et al. A pilot study to evaluate the feasibility of individualized yoga for inpatient children receiving intensive chemotherapy. BMC Complementary and Alternative Medicine. 2015;15(1):2. DOI: 10.1186/s12906-015-0523-9
17. Zahra EN, Maryam R, Abolfazl P, Ghazal Z, Fatemeh M. The effect of aerobic exercise on anxiety in children with cancer. 2017.
18. Liu H, Yin J, Wang K, Liu S, Yang Y, Song Z, et al. Efficacy of physical exercise intervention on children with acute lymphoblastic leukemia during treatment and rehabilitation: a systematic review and meta-analysis. Supportive Care in Cancer. 2024;32(3):177. DOI: 10.1007/s00520-024-08369-7
19. Hosseini S, Abdolshahi M, Ghasemalipour H. The effect of stationary and skill exercises on aggression and depression in working and street children. Sports Psychology. 2019;3:69-84.
20. Paahu A, Tadibi V, Behpour N. The effect of 12 weeks of high-intensity interval training on testosterone, cortisol and lipid profile in inactive overweight and obese boys. Metabolism and Exercise. 2015;5(1):45-58.