FUNCTIONAL OUTCOMES OF AEROBIC AND STRENGTH TRAINING IN CHILDREN WITH CHRONIC LIVER DISEASE

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Abstract

Background: Children with chronic liver disease (CLD) have significant impairment in physical function. Physical deconditioning and sarcopenia are two predictors of morbidity and mortality among children with CLD. Purpose: The present study was conducted to evaluate the effect of aerobic and strength training on aerobic capacity, muscle strength, anthropometric measures (height, weight, body mass index (BMI), triceps skin fold thickness (TST), mid upper arm circumference (MUAC), mid arm muscle circumference (MAMC) and mid upper leg circumference (MULC), health related quality of life (HRQOL) and fatigue in children with CLD.

Methods: Eighteen children with CLD from both sexes aged from 7 to 14 years old included in the study, they were recruited from Hepatology Clinic of Children's Hospital, Cairo University. They received a designed physical therapy program of aerobic and strengthening exercises twice weekly for 8-weeks. The 6-minute walk test, hand held dynamometer (pneumatic and Lafayette hand held dynamometer), anthroplus software, pediatric quality of life inventory core scale and the pediatric multidimensional fatigue scale were used to assess aerobic capacity, grip and quadriceps strength, anthropometric measures, HRQOL and fatigue respectively pre and post treatment.

Results: Comparing the changes from baseline to post-intervention, there was significant improvement in aerobic capacity, grip and quadriceps strength, HRQOL and fatigue ($p < 0.05$). In addition, there was significant improvement in height and weight Post treatment compared to that pretreatment ($p < 0.01$) while, there was no significant change in BMI, TST, MUAC, MAMC and MULC ($p > 0.05$).

Conclusion: Aerobic and strength training can be added to rehabilitation program of children with CLD to improve their aerobic capacity, muscle strength and quality of life.

Keywords: Aerobic training, Chronic liver disease, Functional outcome, Muscle strength.

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Introduction

Chronic liver disease (CLD) is a progressive decline of liver functions for more than 6 months as results of continuous process of hepatocellular inflammation, destruction and regeneration leading to fibrosis and cirrhosis. CLD in children has different prevalence and etiologies that vary with country and age of onset .The most common cause of CLD in infant is biliary atresia and inherited-metabolic disorders, while; liver autoimmune disease and inherited disorder such as Wilson's Disease (WD) are the main causes in children (Widodo et al., 2017).

Aerobic capacity is the ability to consume and use oxygen during exercise which improved after aerobic training and reflected on physical fitness through its impact on multiple systems (cardiovascular, respiratory and neuromuscular). It can be evaluated using different methods, such as the cardiopulmonary exercise test and the 6-minute walk test (6MWT) (Macías-Rodríguez et al., 2019). Children with CLD have impaired exercise capacity as demonstrated as a blunted ability to increase their heart rate or left ventricular ejection fraction during exercise (kruger, 2017).

Muscle power is defined as muscle ability to produce maximal voluntary force or torque (Rhee and Kim, 2015). Quadriceps and grip strength are the most commonly used measures of muscle power that represent whole body muscle strength (Wind et al., 2010). Sarcopenia is a muscle disease characterized by generalized decline of skeletal muscle mass (SMM), strength and physical performance. Prevalence of sarcopenia in children with CLD is common secondary to malnutrition and physical deconditioning (Ooi et al., 2020). Malnutrition is highly prevalent in children with CLD due to their high energy needs for growth. About 25% of children with CLD worldwide have malnutrition with higher incidence in developing countries (Yang et al., 2017). Also, children with CLD have hypercatabolism associated with impaired protein anabolism and low liver cellular function, resulting in hypoalbuminemia that leads to peripheral edema and ascites (Nightingale and Ng, 2009).

Anthropometric measurement is a simple quantitative method of evaluating body composition that reflects nutritional status in children and adults according to the Centers for Disease Control and Prevention (CDC) (Fryar et al., 2016). It is composed of 6 main measurements of height, weight, head circumference, body mass index (BMI), body circumferences and skinfold thickness (Fryar et al., 2016). Children with CLD have decreased arm muscle circumference (AMC) and triceps skin fold (TSF) which correlated with malnutrition and decreased liver functional reserve. There is a strong correlation between nutritional status evaluated by anthropometry and outcomes in children with CLD with a higher risk of mortality and morbidity in children with malnutrition (Prasanna and Giri, 2019).

Health related quality of life (HRQOL) is a multidimensional assessment of disease and intervention impact on patients function and overall health status (Kluetz et al., 2016). The type and severity of CLD may have different effects on HRQOL. Children with liver disease suffer from debilitating fatigue, pruritus, loss of self-esteem, depression, and complications of liver disease (Gulati et al., 2013). Fatigue is felt either at rest or occasionally during or after physical activity due to impaired musculoskeletal function (Nieuwoudt et al., 2017).

Aerobic exercises are modes of physical training that enhance the function of the large muscle group to work continuously and in a synergistic manner (Wahid et al., 2016). It has a beneficial effect on both hepatic function and exercise performance through reduction of hepatic inflammation and adiposity, improved body composition, improved vascular function and higher cardiorespiratory fitness (Thorp and Stine, 2020). Aerobic exercises improve aerobic capacity and may prevent and improve sarcopenia in patients with liver disease (Peterson et al., 2010). Strengthening exercise has been shown to improve SMM, muscle strength, physical performance and quality of life (QOL) in other sarcopenic chronic diseases such as renal, heart and pulmonary failures (Cruz-Jentoft et al., 2014). There is limited research area in the rehabilitation field among children with CLD. Therefore, the scope of the study was to examine the effect of aerobic and strength training on aerobic capacity, muscle strength, anthropometric measures, HRQOL and fatigue in children with CLD.

Methods

Study design and ethical concern

This is a prospective interventional one group study conducted from June 2022 to June 2023 at the outpatient polyclinic, after the approval of Research Ethical Committee at the Faculty of Physical Therapy, Cairo University (P.T.REC/012/004839). Children enrolled after obtaining written informed consent from their parents concerning participation in the current study. The trial was registered with Clinical Trials.gov NCT06240832.

Sample size estimation: It was performed using G*POWER statistical software (version 3.1.9.2; Franz Faul, Universitat Kiel, Germany) with power = 80%, α=0.05, and effect size = 0.77. The required sample size set at 16 subjects based on data of pilot study conducted on 5 subjects assessed hand grip strength.

Study population

Eighteen children with CLD of both sexes have participated in the current study. They were recruited from Hepatology Clinic of Children's Hospital at Cairo University, their age ranged from 7 to 14years old, they had the same socioeconomic status and were medically stable. Children excluded if they had one of the following criteria, fracture of upper and lower limbs, cardiovascular instability and muscle disease as in patient with glycogen storage disease (GSD) or abnormal creatine phosphokinase(CPK), hepatic encephalopathy and or ascites, patients who underwent liver transplantation, patients with end stage liver disease, history of variceal bleeding from one month ago or less, other system disease (chest ,cardiac and nervous system) and children who had hernia.

Children received selected physical therapy program of aerobic and strength training conducted for 8 weeks at twice times/week. Aerobic capacity, muscle strength, anthropometric measures, HRQOL and fatigue were assessed for all children pre and post treatment.

Laboratory and clinical investigation

a-A blood sample was taken for hemoglobin (Hb), liver enzymes (total bilirubin, direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), albumin, prothrombin time (PT), prothrombin concentration (PC), international normalized ratio (INR) and minerals (Na, K, M, Ca, P and create).

b- Pediatric end stage liver disease score (PELD): It is a transparent and objective method that determines patient's candidate for liver transplantation (LT) according to illness severity. PELD score was performed for exclusion of children with end stage liver disease. The PELD score was calculated from liver function test (albumin level, bilirubin level and INR for PT) and growth failure (Chang et al., 2018).

Outcome measures

Aerobic capacity

It was assessed by 6MWT, it is a functional test which has excellent validity and reliability in assessing aerobic capacity in children. It has an intraclass correlation coefficient (ICC) ranged from 0.90 to 0.96 (Li et al., 2005). The test was performed indoors on a level hard surface free from obstacles along a 20-meter straight corridor and marked at 2-meter intervals. Oxygen saturation (Spo2), blood pressure (BP) and heart rate (HR) were tested for all children before and after the test procedure. Children were encouraged to walk as far as possible (without running) at a steady pace for 6 minutes. All children received verbal instructions as permitted by American Thoracic Society guidelines (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002) and informed to stop if they experienced discomfort, dyspnea or other symptoms. The assessor walked behind the child to keep focus during the test without affecting his speed. The distance in meters was recorded at the end of the six minutes according to de Groot et al. (2011).

Muscle strength

Hand grip and quadriceps strength were assessed for all children at the dominant right upper and lower limbs as the following:

A-Hand grip strength: It was assessed by using pneumatic hand held dynamometer (SN.79206754, model 12-0297, USA). It is a valid and reliable tool for assessing grip strength in children with its ICC for inter-rater reliability from 0.95 to 0.97 (Maher et al., 2018). Hand grip strength was measured in pounds per square inch (PSI). The child was sitting on a chair with or without arm rest, back supported, and both feet rested on the floor. The right arm was beside the body, with adducted shoulder, elbow flexed 90°, forearm in neutral position, wrist from 0° to 30° extension, and 0° to 15° of ulnar deviation. Child was instructed to hold and compress the pneumatic handle of dynamometer as much strength as possible with the tested hand. Three consecutive measurements were conducted, and the average was recorded as value of grip strength according to Ferreira et al. (2011).

B-Quadriceps muscle strength: It was assessed by Lafayette handheld dynamometer (LHHD) (Model 01165). LHHD is a portable economic tool that objectively quantifies muscle strength in clinical setting due to its strong reliability and validity with ICC ranged from 0.75 to 0.98 (Hébert et al., 2011; Bohannon., 2012). Child position was sitting on chair with back straight, hip and knee were in 90-degree flexion. LHHD was fixed on distal third of anterior surface of child leg while his/her tested thigh was stabilizing and then the child was instructed to perform maximal isometric knee extension and hold for 6 sec against LHHD sensor pad. Three trials were taken, and their average was recorded according to Katoh et al. (2019); Hébert et al. (2011).

Anthropometric measures

It included the assessment of the following:

A-Weight and height: They were measured for each child by electronic scale and stadiometer.

B- Weight (kg), height (cm) and body mass index (weight/height2) for age were assessed by Anthro plus software version 2007. This software monitors growth in children from 5 to 19 years of age. Weight, height and BMI for age were recorded after entrance of child date of birth, date of evaluation, height and weight which plotted on WHO growth curve (WHO Anthro plus, 2009).

C- Triceps skinfold thickness: It was assessed by Holtain Skinfold Caliper. It is an objective, accurate and reliable tool (ICC of 97.7%) that measure sub-cutaneous fat with measuring range from 0 to 40 mm (Stomfai et al., 2011). It is lighter and easier to hold, thus allowing for repeated measurements with less effort and greater accuracy (Lewandowski et al., 2022). Triceps skinfold thickness (TST) measurements were taken at the right upper arm at the mid-point between acromion and medial and lateral epicondyle according to El Koofy et al. (2019).

D- Mid upper arm circumference (MUAC): It was taken in centimeters (cm) by using non-elastic tape at the right upper arm. Child was sitting relaxed with his/her right upper arm beside body; the tape was passed around the arm at the mid-point of the upper right arm halfway between the acromion process and the olecranon process according to Mazicioglu et al. (2010).

E- Mid arm muscle circumference (MAMC): It is a simple, economic and objective method that calculates somatic protein reserves which considers early indicators of malnutrition. MUAC was measured to the nearest cm, and TST was measured to the nearest millimeter, then MAMC calculated by subtracting TST from the MUAC measurements using MAMC calculators according to Tartari et al. (2013).

F- Mid upper leg circumference (MULC): It was measured by using non-elastic tape at mid -point between iliac crest and mid of patella according to Wong et al. (2019).

Health related quality of life

The Arabic version of child self-report Pediatric Quality of Life Inventory core scale version 4 (PedsQI) was used to assess HRQOL. PedsQI core scale is designed to measure HRQOL in children and adolescents ages from 2 to18 years. It is composed of 23 items comprising 4 domains; physical, mental, social health and school functioning (El-Beh et al., 2018).

All children received a hard copy of the child self-report questionnaire with complete demonstrations of its items. Each item of the questionnaire rated based on a rating scale from 0-4. Then, each item score was linearly converted on assessment scale from 0 to 100;0=100, 1=75, 2=50, 3=25, 4=0 then overall score calculated for all domains through dividing all answered items over whole number of items, with higher scores indicate a better HRQOL according to Arabiat et al. (2011).

Fatigue

It was assessed by the PedsQI multidimensional fatigue scale version 3. It is composed of 3 domains; general fatigue, sleep/rest fatigue and cognitive fatigue (Gordijn et al., 2011). All children had a hard copy of PedsQI multidimensional fatigue scale with complete demonstrations of its questions. Every child rated how often the symptoms occurred during the past month using assessment scale ranging from 0 to 4.Each item score converted on a scale from 0 to 100: 0=100, 1=75, 2=50, 3=25, 4=0 then overall score calculated for all domains through dividing all answered items over whole number of items, with higher scores indicate lower level of fatigue according to Armbrust et al. (2016)

Treatment procedures

All children were instructed to eat additional meals or increase the content of meals, especially protein before and after exercises according to Sirisunhirun et al. (2022). Children received a designed aerobic and strengthening exercise for 8 weeks duration.

Aerobic exercise

It was conducted by using a motorized treadmill (S.N.04065, model 770CE, Italy). Protocol of training started with flexibility exercise for hamstring muscles of both lower limbs in the form of forward lunge and long sitting stretch, treadmill training program consist of 3 phases: warming up for 5 minutes followed by treadmill training at zero inclination and speed of 1.2 kilometers/hour that increased gradually to reach 2.5 kilometers/hour by the end of treatment duration. The duration of treadmill training was 25 -30 minutes that initiated at 5-10 minutes in the first session and increased by 2.5 minutes per session up to 8 weeks, with 5 minutes cooling-down at the end of training (Zenith et al., 2014). All children were monitored during exercise training for any sign of exhaustion in addition, vital signs (Spo2, HR and BP) were monitored before, during and at the end of each session using pulse oximeter and wrist blood pressure monitor. Children were trained at moderate intensity represented by 60-70 % of the maximum HR calculated through Karvonen formula (Fabre et al., 2017).

Strengthening exercises

They were conducted by using Thera band with mild to moderate resistance and free weight (sandbag). They were performed twice a week for 15-20 minutes. Intensity of exercise represented by 70% to 80% of the maximal repetition, three set of 8 repetitions maximum conducted with increasing repetition gradually based on child ability (Zenith et al., 2014).

Exercise included strengthening for both upper and lower limbs in the form of; push up exercise, strengthening of shoulder horizontal abductors using Thera band, strengthening of elbow flexors, and extensors and knee extensors muscles by using free weight, squatting and jumping exercises. The first session began with 5-10 repetition for each exercise that increased gradually every week based on child tolerance and ability, maximum number of repetitions reached 30-40 repetition (Contreras et al., 2012; Vanhees et al., 2012; Kushner et al., 2015; Kramer et al., 2017 and Hewett et al., 2002).

Home-based exercise

All children performed home based exercise and received instructions and precautions regarding exercise. Children received a hard copy of the home program that included exercise description and repetition per week (3 times per week for 8 weeks on days away from site-based program). Children and parents were instructed to stop exercise for any sign of dyspnea or leg pain. Exercise repetition increased gradually according to child ability with close monitoring of parents and frequent phone call to ensure safety and adherence to home program. Home based exercise program included stretching, independent walking, jumping, squatting and push-up exercise.

Statistical analysis

Descriptive statistics of mean, standard deviation and frequency were conducted for expression of subject characteristics of the study group. The Shapiro-Wilk test was used to check normal distribution of data. Paired t test was conducted for comparison between pre and Post for normally distributed data. All statistical analysis was conducted using the statistical package for social sciences (SPSS) version 25 for windows with significance level for statistical tests was set at $p < 0.05$.

Results

Subject characteristics

Eighteen children with CLD participated in this study. Their mean ± SD age, weight, height and BMI were 10 ± 3.01 years, 29.81 ± 8.19 kg, 130.94 ± 14.08 cm and 17.04 ± 1.59 kg/m² respectively. Participant characteristics are presented in (Table 1). In the current study there were 22% of patients had history of variceal bleeding, 11% on B blockers, 11% on steroids, with general examination 11% had pallor, 27% had clubbing, 11% had history of edema in lower limb, 5% orthopnia, 11% platepnea,27% had history of cyanosis during crying or angry, 50% had anorexia and 61% had fatigue.

Comparison of anthropometric measures between pre and post treatment:

Height and weight values of the study group were significantly increased post treatment compared with that pretreatment ($p < 0.01$) while BMI, TST, MUAC, MAMC and MULC did not change significantly ($p > 0.05$) (Table 2).

Comparison of Hb, liver function test and minerals between pre and post treatment:

Blood sample test of Hb, liver function test and minerals did not change significantly post treatment ($p > 0.05$) (Table 3).

Comparison of aerobic capacity, muscle strength, health related quality of life and fatigue between pre and post treatment

There was a significant increase in 6MWT, hand grip and quadriceps strength, PedsQI and PedsQI multidimensional fatigue score post treatment compared with that pretreatment ($p < 0.05$). (Table 4).

Discussion

The present study was designed to evaluate the effectiveness of aerobic and strength training on aerobic capacity, muscle strength, anthropometric measures, HRQOL and fatigue in children with CLD.

Chronic liver disease (CLD) in children is associated with progressive decline in liver structure and function due to continuous process of inflammation, fibrosis, cholestasis and hepatocellular necrosis (Zhou et al., 2014). Children with CLD have a significant decline in aerobic capacity, muscle strength and HRQOL. They display very low levels of physical activity and have altered exercise physiology with impairment in aerobic capacity (Lemyze et al., 2013).

The current study considers one of few studies that examined the effect of exercise intervention in children with liver disease, most previous studies either examined children's level of physical activity after liver transplantation (LT) compared with healthy children like the study conducted by Bos et al. (2019) on children after LT or examined the effect of exercise on adult populations with liver disease.

The results of the current study showed that there was significant improvement in aerobic capacity, grip, and quadriceps strength, HRQOL and fatigue after the treatment protocol. In addition, there was significant improvement in height and weight post treatment compared to that pretreatment while there was no significant change in BMI, TST, MUAC, MAMC and MULC.

The post treatment improvement in aerobic capacity among children with CLD could be due to improving their muscular strength and ability to perform endurance activity like walking, also improving skeletal muscle circulation and ability to use oxygen. This is supported by De Moor and Ramblers, (2013); Zenith et al. (2014) who documented that aerobic exercise like walking improves aerobic capacity through enhancing skeletal muscle vascularity and oxygen extraction by the contracting muscles. Holland et al. (2010) had showed that

Table 1. Participant characteristics.

	Mean ± SD	Minimum	Maximum
Age (years)	10 ± 3.01	7	14
Weight (kg)	29.81 ± 8.19	19	45.2
Height (cm)	130.94 ± 14.08	111	156
BMI (kg/m²)	17.04 ± 1.59	14.1	20.1
	N	**%**	
Sex distribution			
Girls	4	22	
Boys	14	78	
Diagnosis			
Autoimmune hepatitis (AIH)	3	16.7	
AIH and Crohins	1	5.6	
Alagille	2	11.1	
Chronic hepatic fibrosis (CHF)	3	16.7	
Cholestasis	3	16.7	
Fatty liver	1	5.6	
Hepatitis C Virus (HCV)	1	5.6	
Wilson's disease (WD)	4	22.2	
Hepatomegaly	10	55.55	
Splenomegaly	7	38.88	

SD, Standard deviation

Table 2. Comparison of anthropometric measures between pre and post treatment.

	Pre	Post	MD	% of change	t- value	p-value
	Mean ± SD	Mean ± SD				
Height (cm)	130.94 ± 14.08	132.55±14.47	-1.61	1.23	-3.31	**0.004**
Weight (kg)	29.81 ± 8.19	30.76 ± 8.45	-0.95	3.19	-3.58	**0.002**
BMI (kg/m²)	17.04 ± 1.59	17.15 ± 1.87	-0.11	0.65	-0.67	**0.51**
TST (mm)	7.33 ± 2.93	6.56 ± 3.24	0.77	10.50	1.74	**0.1**
MUAC (cm)	18.06 ± 2.63	18.56 ± 2.85	-0.5	2.77	-1.73	**0.1**
MAMC normal	11(61%)	12(67%)				**1**
MAMC abnormal	7(39%)	6(33%)				**1**
MULC (cm)	36.06 ± 4.92	35.89 ± 5.32	0.17	0.47	0.5	**0.62**

SD, Standard deviation; MD, Mean difference; p value, Probability

Table 3. Comparison of Hb, liver function test and minerals between pre and post treatment.

	Pre	P0st	MD	% of change	t- value	p-value
	Mean ± SD	Mean ± SD				
Hb (g/dl)	11.47 ± 1.28	11.36 ± 1.26	0.11	0.96	0.55	**0.59**
Albumin (g/dl)	4.49 ± 0.48	4.44 ± 0.39	0.05	1.11	0.52	**0.61**
Total bilirubin (mg/dl)	0.71 ± 0.45	0.89 ± 0.94	-0.18	25.35	-0.98	**0.33**
Direct bilirubin (mg/dl)	0.25 ± 0.23	0.27 ± 0.26	-0.02	8	-1.1	**0.28**
AST (U/L)	82.33 ± 86.76	63 ± 45.37	19.33	23.48	1.17	**0.25**
ALT (U/L)	74.44 ± 74.23	63.75 ± 55.39	10.69	14.36	1.16	**0.26**
ALP (U/L)	416.83 ± 233.60	376.77 ± 212.37	40.06	9.61	1.33	**0.2**
GGT (U/L)	132.39 ± 145.51	132.94 ± 140.25	-0.55	0.42	-0.09	**0.92**
PT (s)	14.55 ± 3.93	14.39 ± 3.94	0.16	1.10	0.59	**0.55**
PC (s)	85.99 ± 18.54	85.82 ± 18.33	0.17	0.20	0.12	**0.91**
INR %	1.15 ± 0.31	1.14 ± 0.29	0.01	0.87	0.95	**0.35**
Na (mmol/l)	136.28 ± 2.14	137.42 ± 3.15	-1.14	0.84	-1.33	**0.20**
K (mmol/l)	4.16 ± 0.45	4.23 ± 0.43	-0.07	1.68	-0.56	**0.57**
Ca (mg/dl)	8.63 ± 1.40	8.68 ± 1.47	-0.05	0.58	-0.25	**0.80**
Mg (mg/dl)	2.57 ± 0.88	2.34 ± 0.31	0.23	8.95	1.16	**0.26**
Phosphorus (mg/dl)	4.63 ± 0.81	4.74± 0.72	-0.11	2.38	-0.84	**0.41**
Creatinine (mg/dl)	0.58 ± 0.29	0.62 ± 0.23	-0.04	6.90	-0.89	**0.38**

SD, Standard deviation; MD, Mean difference; p value, Probability

Table 4. Comparison of 6MWT, muscle strength, PedsQI and PedsQI multidimensional fatigue score between pre and post treatment.

	Pre	P0st	MD	% of change	t- value	p-value
	Mean ± SD	Mean ± SD				
6MWT (m)	412.93±52.29	438.51±57.6	-25.58	6.19	-2.29	**0.03**
Grip strength (PSI)	2.99±1.35	3.90±1.77	-0.91	30.43	-3.81	**0.001**
Quadriceps strength (LBS)	2.98 ± 1.25	3.61±1.62	-0.63	21.14	-2.48	**0.02**
PedsQI score	72.79±15.27	81.93±11.74	-9.14	12.56	-3.47	**0.003**
PedsQI multidimensional fatigue score	69.31±18.67	77.06±15.72	-7.75	11.18	-2.37	**0.03**

SD, Standard deviation; MD, Mean difference; p value, Probability.

minimal important difference for the 6MWT to improve functional outcome was 25-30 meter which is consistent with the current result in which the walking distance increased by 25.58 m as measured by 6MWT and in agreement with study conducted on patients with chronic obstructive pulmonary disease in which 6MWT increased by 14% following combined site and home based exercise program (De Roos et al., 2018) .Also the improvement in the current aerobic capacity is consistent with studies conducted by Román et al .(2014) ;Williams et al.(2015) ; Moya-Nájera et al.(2017) that examined effect of aerobic exercise on patients with cirrhosis, patients listed for LT and patients with LT and reported significant improvement in both 6MWT and vo2peak. On the opposite hand this result inconsistence with the result of study conducted on patients with cirrhosis found no improvement in aerobic capacity that evaluated by cardiopulmonary exercise test (Román et al., 2016), this could be due to population of the current study was children with CLD with low severity than adult with cirrhosis.

Regarding post treatment improvement in grip and quadriceps strength, this improvement could be related to weight added and Thera band use that result in improving skeletal muscle performance. Which is supported by Aagaard et al. (2002) who reported that resistance training can improve muscle performance without increase muscle mass through improving neurological function in the form of increased central motor drive and elevated motor neuron excitability. This result is consistence with result of previous studies conducted by Morkane et al. (2020); Debette-Gratien et al. (2015) who investigated effect of aerobic training alone and combined aerobic and strength training on patients waiting for LT and showed significant improvements in hand grip and quadriceps strength.

Outcomes of anthropometric measures showed significant improvement in height and weight post treatment, while there was no significant difference in the other anthropometric measurements (BMI, TST, MUAC, MAMC and MULC) which may be due to duration and intensity of resistance training are not enough to make physiological change to increase muscle mass and decrease arm fat as measured by arm, leg circumference and triceps skin fold. In a previous study of Nelson et al. (2007) demonstrated the importance of physical activity in promoting muscle hypertrophy and strength gain through gradual progression of intensity by increasing load as determined by American College of Sports Medicine's and Americans Heart Association's guidelines. Statistically significant improvement in height and weight post treatment could be related to all children in the current study performed regular exercise program with good nutrition that could promote protein anabolism which reflected on child growth. This is supported by Shimomura et al. (2004); Beaulieu et al. (2020) who documented that exercise with inadequate diet promotes protein catabolism. This agrees with pilot study conducted by Román et al. (2014) on 17 patients with cirrhosis and they found a statistically significant increase in their body weight.

In addition, there was statistically significant improvement in HRQOL and fatigue scores post treatment that might be related to improvement in aerobic capacity and muscle strength which result in improving and maintaining children autonomy and allow them to be able to perform activities of the daily living. This is supported by Vuille-Lessard and Berzigotti, (2022);Chow et al. (2022) who reported that physical exercise has a favorable effect on fatigue, depression and anxiety which indirectly improves QOL, as well as brain release mediators in response to exercise that enhance overall health status .This result agrees with studies conducted by Moya-Nájera et al. (2017); Román et al. (2014) who assessed the effect of physical exercise on HRQOL on patients with LT and cirrhosis and they found significant improvement in all domains of health status.

Also, there was no significant change of laboratory investigations in comparison to base line which could be related to short duration of exercise. This is supported by de Piano et al. (2012) who showed that combined aerobic and resistance exercise have positive effect on liver enzymes after regular exercise for a long duration. On the opposite hand, the study conducted by Shamsoddini et al. (2015) found 8 weeks of aerobic exercise reduce the serum AST and ALT levels which inconsistent with the results of the current study.

Limitations

The current study had several limitations such as small sample size and lack of sample stratification according to etiologies. So, future randomized clinical trials of larger sample size that investigate the effect of physical exercise on functional outcomes in children with CLD are recommended.

Implications for physiotherapy practice

Aerobic and strength training are considered effective rehabilitation modalities for children with CLD, as they have a favorable impact on aerobic capacity, muscle strength, weight, height, HRQOL, and fatigue.

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Conflict Of Interest Statement

The authors have no conflicts of interest to declare

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