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ORIGINAL ARTICLE

Effect of resistance and aerobic exercises on bone mineral density, muscle strength and functional ability in children with hemophilia

Mohamed A. Eid [a,*], Marwa M. Ibrahim [a], Sobhy M. Aly [b]

[a] *Department of Physical Therapy For Growth and Development Disorders in Children and Its Surgery, Faculty of Physical Therapy, Cairo University, Cairo, Egypt*
[b] *Department of Biomechanics, Faculty of Physical Therapy, Cairo University, Cairo, Egypt*

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Abstract *Background and purpose:* Children with hemophilia are at risk for reduced bone mineral density (BMD), muscle strength and functional ability as a result of reduced leisure-time activity and less involvement in intense activities. So, the purpose of this study was to investigate the effect of resistance and aerobic exercise program on BMD, muscle strength and functional ability in children with hemophilia.

Materials and methods: Thirty boys with hemophilia A ranging in age from 10 to 14 years had participated in this study. They were assigned randomly into two equal groups (control and study groups). Control group received a designed physical therapy program and aerobic exercise in the form of treadmill training, while the study group received the same program as the control group in addition to resistance training program in the form of bicycle ergometer training and weight resistance. Both groups received treatment sessions three times per week for three successive months. BMD, muscle strength of knee flexors and extensors and functional ability were evaluated before and after the 3 months of treatment program.

Results: There was no significant difference between both groups in the pre-treatment mean values of all measured variables. Significant improvement was observed in BMD, knee extensors and flexors strength, and functional ability in the study group when comparing pre and post treatment

* Corresponding author. Address: El-Shiekh Zayed City, Region 13, Neighboring 3, Building 59A, 6th October City, Giza, Egypt. Tel.: +20 238953447/1000644601.
E-mail address: mohamed.eid27@yahoo.com (M.A. Eid).

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measurements. There was a significant improvement in functional ability of the control group. Significant difference was also observed between both groups when comparing the post treatment measurements in favor of the study group.

Conclusion: Based on obtained data, it can be concluded that, resistance and aerobic exercise training program is effective in increasing BMD, muscle strength and functional ability in children with hemophilia.

1. Introduction

Hemophilia is an X-linked inherited recessive bleeding disorder that is characterized by a deficiency of clotting factor VIII (classic hemophilia, or hemophilia A) or IX (hemophilia B). Hemophilia "A" has a frequency of 1 in 5000 male births, where hemophilia "B" has a frequency of 1 in 30,000 male births [1]. The severity of the disease depends upon the level of clotting factor activity. Children with severe hemophilia (clotting factor activity $<1\%$) are characterized by spontaneous bleeding, moderately affected children (clotting factor activity 1–5%) have a great risk of bleeding with minor trauma and children with mild hemophilia (clotting factor activity 5–40%) bleed excessively only during surgery or trauma [2].

Because of hemarthroses, subsequent synovitis and arthropathy, children with hemophilia often have a sedentary lifestyle [3]. Although, children are more active than adults, children with hemophilia are at risk of developing hypokinesia due to decreased motor fitness and passive leisure activities [4]. Also, children with hemophilia often avoid any physical activity in their everyday life as a result of parental or medical restrictions. Therefore, active lifestyle is essential to maintain musculoskeletal health, reduce the risk of complications and ensure better quality of life in patients with hemophilia [5]. It was recognized that the attitude toward sports among children with hemophilia has improved, and the range of sports practiced has increased, as a result of improved medical treatment [6,7].

Despite increasing sport activity, children with hemophilia still tend to be less physically fit than their healthy peers. Physical fitness of children with hemophilia whose age ranged from 8.3 to 15.5 years was evaluated by Koch et al. [8] and reported a significant reduction in exercise capacity, possibly because of insufficient intensity of daily physical activities. Also, children with hemophilia have a decreased aerobic capacity and decreased ability to involve in higher intensity activities compared to their healthy peers [9]. Children with hemophilia often demonstrate a significant reduction in muscle strength and anaerobic power, especially in the lower limbs [10]. Furthermore, decreased activity level may result in overweight or obesity in children with hemophilia because of joint bleedings and overprotection [11]. The need for a physically active lifestyle in hemophilic children is further highlighted by the finding that bone mineral density (BMD) in children with hemophilia is lower than in healthy peers [12]. Also Falk et al. [13] reported a lower muscular anaerobic power and dynamic strength among children with hemophilia compared with age-matched controls. The reduced muscular performance capacity among children with hemophilia was explained by a lower level of physical activities in which lower performance capacity was apparent in both lower and upper limbs. Muscle weakness reduces bone loading, leading to demineralization and osteoporosis [14,15].

Children with hemophilia, who are less physically active than healthy peers, often suffer from acute or chronic orthopedic injuries which may further limit their physical activities. Indeed, it was noted that the lower level of physical fitness in hemophilic children was associated with reduced muscular strength [13]. So, the purpose of this study was to determine the effect of resistance and aerobic exercise training program on BMD, muscle strength and functional ability in children with hemophilia.

2. Materials and methods

2.1. Subjects

Thirty boys with hemophilia A whose ages ranged from 10 to 14 years were enrolled in this study. They were selected from Abo El-Rish pediatric hospital, Cairo university hospitals, Cairo, Egypt and assigned randomly into two equal groups (control and study groups). Children in both groups were under medical treatment in the form of replacement therapy with recombinant factor VIII which is considered the first and essential step in the treatment of hemophilia. The work is carried out in accordance with The code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Parents of the children signed a consent form prior to participation as well as acceptance of the Ethics Committee of the University was taken.

All patients in both groups were selected according to the following inclusion criteria:

(1) Patients who were diagnosed as having moderate hemophilia.
(2) Patients who were free from severe tightness or any congenital deformities or cardiopulmonary dysfunctions.

Exclusion criteria:

(1) Patients with advanced radiographic changes as bone erosions, destruction, bony ankylosis or joint subluxation.
(2) Children who had surgical procedures performed six weeks prior to or during the exercise program.

2.1.1. Control group

Consisted of fifteen children who received a designed physical therapy program in the form of:

- Gentle stretching exercises for tight muscle groups around elbow, knee and ankle joints for 15 min.

- Static muscle contraction for quadriceps, hamstrings, anterior tibial group, calf muscles, biceps brachii and triceps for 15 min.
- Aerobic exercise in the form of treadmill training for 30 min.

This program was applied for 1 h, three times per week for three successive months.

2.1.2. Study group

Consisted of fifteen children who received the same program as the control group in addition to resistance training program in the form of:

- Bicycle ergometer training for 20 min.
- Resistance exercises through weight resistance (sand bags) for 20 min.
- The total program lasted one hour and 40 min applied three times per week for three successive months.

2.2. Materials

2.2.1. For evaluation

2.2.1.1. Height and weighting scale. It was used for measuring height and weight of each child. Body mass index (BMI) was calculated using the standard formula: mass (kg)/height^2 (m).

2.2.1.2. Dual Energy X-ray Absorptiometry (DEXA). Dual energy X-ray absorptiometry (DEXA) was used for the evaluation of BMD which consists of a central device with a padded platform and a mechanical arm (scanner) that is adjusted to emit low dose X-ray on the area required to be measured and X-ray generator. The equipment is combined with a computer device with a specific software to determine BMD. DEXA is the most common method for assessing BMD in children and must take into consideration age, height, weight and sexual maturity rating [16]. It has been extensively used to evaluate BMD and to monitor the effects of treatment on bone sites [17]. It has high precision, low irradiation dose and fast scanning time [18].

2.2.1.3. Isokinetic dynamometer. The Biodex System 3 multi-joint system testing and rehabilitation (Biodex Medical System, Shirley, NY, USA) was used to measure knee flexors and extensor peak torque. The system consists of head assembly housing the servomotor responsible for moving the lever arm and has a fully adjustable orientation, seat for positioning the subject that adjusted independently vertical or horizontal, and control unit consisting of personal computer and operator equipment. Velocity, range of motion (ROM) setting, and contraction mode are addressed through the system controller. Dynamometry attachments are selected according to the tested part. Previous studies have demonstrated the reliability and validity of isokinetic devices for measuring muscle strength in adults as well as in children [12].

2.2.1.4. Six Minute Walk Test (6MWT). Six minute walk test (6MWT) is a sub-maximal test of aerobic capacity, in which subjects walk as far as possible in 6 min around a pre-measured distance. It is a useful assessment tool for children with chronic conditions affecting the musculoskeletal system, because walking is a part of their everyday life [19]. It is also used to measure walking ability and baseline cardiovascular function of people with disease or low levels of fitness [20].

2.2.2. For treatment

2.2.2.1. Treadmill. Treadmill apparatus (En Tred) is a steel structure 2.4 m long, and ½ m width and is formed of a belt, two cylinders, and an axle along its width. The treadmill belt is a loop of synthetic rubber and nylon 3.75 m long that passes around 2 cylinders of 0.31 m in diameter. Parallel bars are attached on vertical beams at each side of the apparatus and its height was adjusted according to each child.

2.2.2.2. Bicycle ergometer. Bicycle ergometer (Monark Rehab Trainer model 88 IE) is an electronically braked ergometer. It is equipped with an electronic meter showing pedal revolutions per minute, the total pedal revolution and time function. The bicycle is supplied by pedal strap to provide complete fixation of the child's foot and back support in order to support and prevent over exhaustion of back muscles. It has a monitor that shows the heart rate of the child in order to control the exercise intensity and well stabilized by wide base of support, so that the child was trained with maximum safety.

2.3. Methods

2.3.1. For evaluation

2.3.1.1. Bone mineral density. Each child in both groups was evaluated before and after the 3 months of treatment by DEXA for measuring BMD of the femoral neck, proximal tibia and distal tibia, using a standard technique for measuring bone mineral content with a very low dose of radiation of acceptable precision using bone mineral content in grams (g) by area of bone measured (cm^2) and will express density as g/cm^2.

2.3.1.2. Muscle strength. Knee flexors and extensors of the dominant side were measured during concentric contraction at 120°/s. These muscle groups were chosen because they are involved in the joint mostly affected in hemophilia. Approximately 80% of recurrent hemarthroses occur in this diarthroidal joint [21], most often in the lower limbs [13].

- *For hamstrings and quadriceps:* the dynamometer orientation was adjusted according to the standard instructions for knee testing so that the dynamometer head and chair were rotated to 90°. Subjects sat with their thighs at an angle of 110° to the trunk. With the tested knee positioned at 90° flexion, the mechanical axis of the dynamometer was aligned with the lateral epicondyle of the knee. The trunk and both thighs were stabilized with belts and the knee range of motion was 90° (90–0° of flexion). The distal aspect of the dynamometer arm was placed 2 cm proximal to the medial malleolus, torque was gravity corrected and dynamometer calibration was performed before every session in accordance with the manufacturers' instructions. Each subject performed 10 concentric contractions at 120°/s (flexion and extension) and peak torque of knee flexors and extensors were recorded.

2.3.1.3. Functional ability. Functional ability was determined by means of 6MWT [22]. Children were allowed to walk on an unobstructed, rectangular pathway following the guidelines of the American Thoracic Society. To ensure safety and to measure the exact distance walked in 6 min, the therapist followed closely with a stopwatch. The walking course distance of 20 m between turning points was used. Each child was instructed to cover as many laps of the course as possible in 6 min without running [23].

2.3.2. For treatment

Control group received a designed physical therapy program in the form of:

A- Gentle stretching exercises for biceps brachii, hamstrings and calf muscles bilaterally. It was applied for 20 s stretch followed by 20 s relaxation and repeated five times per session for each muscle, for 15 min.

B- Static muscle contraction for quadriceps, hamstrings, anterior tibial group, calf muscles, biceps and triceps for 15 min. Static muscle contraction was performed five times initially, building up to 10 repetitions as tolerated, two to three times per day [15,24]. Each contraction was maintained five counts then relaxed for another five counts for five times per session.

- *For quadriceps:* the child was lying supine with extended both lower limbs and a small pillow was placed under the affected knee joint and the child was asked to press maximally over the pillow.
- *For hamstrings:* the child was lying supine with extended both lower limbs and asked to press maximally over the bed by the heel of the affected limb.
- *For anterior tibial group:* the child was lying supine with extended both lower limbs and asked to bring the ankle into dorsiflexion and contract anterior tibial group maximally as if he maintain dorsiflexion.
- *For calf muscles:* the child was lying supine with extended both lower limbs and a pillow was placed between his feet and the edge of the bed, then the child was asked to press maximally over the pillow.
- *For biceps brachii:* the child sat in a comfortable position and was asked to contract the biceps muscle maximally as if he bend his elbow but without movement.
- *For triceps muscle:* the child sat in a comfortable position and was asked to maintain elbow extension and contract triceps muscle maximally as if he extend his elbow but without movement.

C- Aerobic exercise in the form of treadmill training for 30 min: The procedure and goals of exercise were explained to all children before starting walking on treadmill. Children grasped both parallel bars of the treadmill by both hands firmly and asked to look forward and do not look downward on their feet during walking as this may cause falling. The exercise training consisted of 5 min of warm-up exercises involving light stretch and walking back and forth inside the room then dynamic aerobic exercise over treadmill was begun. A comfortable treadmill speed was selected for all children in both groups as 75% of their comfortable speed during over ground walking and zero degree inclination for 20 min [25,26]. The child was instructed to stop walking immediately if he felt pain, fainting, or shortness of breath. Finally, cooling down exercises for 5 min involving light stretch and walking inside the room were performed.

Study group received the same program that was given to the control group, with 5 min rest after completing the program in addition to resistance training program in the form of:

A- Bicycle ergometer training for 20 min: Children were asked to sit on the seat of the bicycle with straight and supported back. Then, fixation of both feet by pedal straps was performed. The child was asked to grasp handles of the bicycle by both hands firmly to provide stability during training. Climb steady program was selected in which resistance has been increased gradually according to muscular force. Applying resistance comes in agreement with the results that confirmed the necessity of resistance training for children with hemophilia as they have demonstrated lower levels of anaerobic capacity and strength when compared with healthy children [13]. The child was asked to perform pedaling on a bicycle ergometer starting at lower intensity for 5 min as a warming up. Then, the child performed pedaling while gradually increasing resistance for about 10 min and end the treatment session with unloaded cycling for another 5 min as a cooling down. The child was instructed to immediately stop exercising if he felt pain, fainting or shortness of breath.

B- Resistance exercise training for 20 min: It was individually tolerated and applied for quadriceps and hamstrings in the form of weight resistance (sand bags from 2 to 6 kg). Initially, a small weight was used and children performed sets of repetitions starting at 3 sets of 10 repetitions and progressed to 3 sets of 15 repetitions with 2 min rest period in between until the amount of weight lifted was no longer challenging. Then, the repetitions started again at 3 sets of 10 repetitions at the new weight level [27]. Children were instructed to move the part against weight within their limits of pain and muscle fatigue [28]. The number of times the child lifted the weight through full ROM before getting fatigue was recorded as equivalent repetition maximum (RM) [29].

For quadriceps femoris muscle: the child was instructed to sit in a high sitting position with back support angle of 120° to place the rectus femoris in a stretched position, therefore, causing the force of knee extensors to be increased [30]. Trunk was strapped to back support and the thigh was also strapped to the seat just above knee joint to avoid substitution. Suitable sand bag was strapped on the lower leg just above ankle joint and the child was instructed to move the leg from 90° knee flexion to full knee extension.

For hamstring muscle: the child was lying prone on a plinth with both feet outside the edge of the plinth. A pillow was placed under both knees to prevent friction of knee joint with the plinth. Pelvis and thighs were strapped to the plinth to prevent substitution. Sand bag was strapped on the posterior aspect of the leg just above the ankle joint and the child was instructed to bend the leg from full knee extension to full flexion.

2.4. Measurements

BMD, muscle strength and functional ability were evaluated prior to the beginning of training and took place immediately after ending the 3 months of training program.

2.5. Statistical analysis

The collected data of BMD, muscle strength and functional ability of both groups were statistically analyzed to study the effect of resistance and aerobic exercise training on all the measuring variables in hemophilic children. The age, weight, height and BMI were expressed as mean ± standard deviation. *T* test was conducted for comparing the pre and post treatment mean values of all measuring variables between both groups. Paired *T* test was conducted for comparing pre and post treatment mean values in each group. All statistical analyses were conducted through SPSS (statistical package for social sciences, version 19).

3. Results

3.1. Subject characteristics

Table 1, showed the mean ± SD age, weight, height, and BMI of control and study groups. There was no significant difference between both groups in the mean age, weight, height, and BMI ($p > 0.05$).

3.2. Bone mineral density

There was no significant difference between control and study groups in BMD pre-treatment ($p > 0.05$). Comparison between control and study groups post treatment revealed that there was a significant increase of BMD of femoral neck, proximal tibia and distal tibia in the study group compared to the control group ($p < 0.05$) (Table 2).

There was a significant increase in BMD of femoral neck, proximal tibia and distal tibia post treatment in the study group ($p < 0.05$), while there was no significant difference in the control group between pre and post treatment ($p > 0.05$) (Table 3).

3.3. Muscle strength

There was no significant difference between control and study groups in muscle strength pre-treatment ($p > 0.05$). There was a significant increase in strength of knee extensors and flexors in the study group compared to the control group post treatment ($p < 0.05$) (Table 4).

There was a significant increase in muscle strength of knee extensors and flexors in the study group post treatment compared to pre-treatment ($p < 0.05$), the control group showed no significant difference in muscle strength between pre and post treatment ($p > 0.05$) (Table 5).

3.4. Functional ability

There was no significant difference between control and study groups in functional ability pre-treatment ($p > 0.05$). Also, there was no significant difference between both groups in mean value of 6MWT post treatment ($p > 0.05$). (Table 6).

There was a significant increase in 6MWT score post treatment compared to pre- treatment in both groups ($p < 0.05$) (Table 7).

4. Discussion

Physical activity during childhood and adolescence is essential for health as well as social reasons. Children with hemophilia are less physically active compared with healthy peers. This low activity level may influence their physical capacity, muscular ability and bone strength [13]. Also, children with hemophilia who are less active than their healthy peers generally have decreased muscle strength and flexibility, and have lower aerobic working capacity [31]. For this reason, the current study was designed to investigate the effect of resistance and aerobic exercise training on BMD, muscle strength and functional ability in children with hemophilia.

The pre and post-treatment results of the control group showed that there was no significant difference in BMD and muscle strength but significant improvement was obtained in functional capacity. On the other hand, there was a significant improvement in the study group in all measuring variables which could be attributed to the combined effect of resistance and bicycle ergometer training.

These results came in agreement with Hilberg et al. [10] and Skinner et al. [32] who emphasized that regular physical activity is extremely essential for hemophilic children as it results in such benefits, as increase in muscle strength, flexibility, skeletal muscle cross-sectional area and decreased body fatness. Physical training also has a protective value as it reduces the risk of development of several diseases, increases BMD, improves self-image, cardiovascular fitness, joint stabilization and coordination.

Table 1 *T* test for comparison between control and study groups in mean age, weight, height, and BMI.

	Study $\overline{X} \pm SD$	Control $\overline{X} \pm SD$	*t*-Value	*p*-Value
Age (years)	12 ± 1.36	12.13 ± 1.35	−0.26	0.79*
Weight (kg)	38.06 ± 4.54	37.66 ± 5.43	0.21	0.82*
Height (cm)	132.13 ± 4.59	136.33 ± 8.85	−1.63	0.11*
BMI (kg/cm^2)	21.75 ± 1.93	20.31 ± 2.55	1.74	0.09*

$\overline{X}$, Mean; SD, standard deviation; *p*-value, level of significance.
* Non-significant.

Table 2 *T* test for comparison of pre and post treatment mean values of BMD between both groups.

BMD (g/cm^2)		Study group $\overline{X} \pm SD$	Control group $\overline{X} \pm SD$	*t*-Value	*p*-Value
Pre	Femoral neck	0.59 ± 0.17	0.68 ± 0.13	−1.47	0.15*
	Proximal tibia	0.58 ± 0.1	0.63 ± 0.12	−1.06	0.29*
	Distal tibia	0.37 ± 0.08	0.4 ± 0.07	−0.99	0.33*
Post	Femoral neck	0.86 ± 0.12	0.73 ± 0.16	2.55	0.01**
	Proximal tibia	0.74 ± 0.1	0.637 ± 0.13	2.61	0.01**
	Distal tibia	0.54 ± 0.1	0.46 ± 0.1	2.05	0.04**

$\overline{X}$, Mean; SD, standard deviation; *p*-value, level of significance.
* Non significant.
** Significant.

Table 3 Paired *T* test for comparison of pre and post treatment mean values of BMD in each group.

BMD (g/cm^2)		Pre $\overline{X} \pm SD$	Post $\overline{X} \pm SD$	*t*-Value	*p*-Value
Study group	Femoral neck	0.59 ± 0.17	0.86 ± 0.12	−6.15	0.0001**
	Proximal tibia	0.58 ± 0.1	0.74 ± 0.1	−9.2	0.0001**
	Distal tibia	0.37 ± 0.08	0.54 ± 0.1	−12.99	0.0001**
Control group	Femoral neck	0.68 ± 0.13	0.73 ± 0.16	−1.92	0.07*
	Proximal tibia	0.63 ± 0.12	0.637 ± 0.13	−1.91	0.07*
	Distal tibia	0.4 ± 0.07	0.46 ± 0.1	−1.08	0.29*

$\overline{X}$, Mean; SD, standard deviation; *p*-value, level of significance.
* Non significant.
** Significant.

Table 4 *T* test for comparison of pre and post treatment mean values of isokinetic strength between both groups.

Peak torque (N.m)		Study group $\overline{X} \pm SD$	Control group $\overline{X} \pm SD$	*t*-Value	*p*-Value
Pre	Knee extensors	51.2 ± 14.13	55.42 ± 14.39	−0.81	0.42*
	Knee flexors	22.32 ± 8.92	23.73 ± 11.98	−0.36	0.71*
Post	Knee extensors	70.22 ± 14.43	55.8 ± 14.02	2.77	0.01**
	Knee flexors	33.31 ± 8.67	24.01 ± 12.15	2.41	0.02**

$\overline{X}$, Mean; SD, standard deviation; *p*-value, level of significance.
* Non significant.
** Significant.

Table 5 Paired *T* test for comparison of pre and post treatment mean values of isokinetic strength in each group.

Peak torque (N.m)		Pre $\overline{X} \pm SD$	Post $\overline{X} \pm SD$	*t*-Value	*p*-Value
Study group	Knee extensors	51.2 ± 14.13	70.22 ± 14.43	−16.26	0.0001**
	Knee flexors	22.32 ± 8.92	33.31 ± 8.67	−13.89	0.0001**
Control group	Knee extensors	55.42 ± 14.39	55.8 ± 14.02	−1.54	0.14*
	Knee flexors	23.73 ± 11.98	24.01 ± 12.15	−0.61	0.55*

$\overline{X}$, Mean; SD, standard deviation; *p*-value, level of significance.
* Non significant.
** Significant.

The results obtained from this study revealed that there was a significant improvement in BMD in the study group compared with the control group. This can be attributed to the effect of resistance and aerobic exercises on increasing bone mineral content and this comes in agreement with Kohrt et al. [33] who evaluated the osteogenic response in rats to several

Table 6 *T* test for comparison of pre and post treatment mean values of 6MWT between both groups.

6MWT (m)	Study group $\overline{X} \pm SD$	Control group $\overline{X} \pm SD$	*t*-Value	*p*-Value
Pre	274.66 ± 36.02	281.66 ± 36.62	−0.52	0.6*
Post	301.66 ± 40.86	295.66 ± 35.39	−0.43	0.67*

$\overline{X}$, Mean; SD, standard deviation; *p*-value, level of significance.
* Non significant.

Table 7 Paired *T* test for comparison of pre and post treatment mean values of 6MWT in each group.

6MWT (m)	Pre $\overline{X} \pm SD$	Post $\overline{X} \pm SD$	*t*-Value	*p*-Value
Study	274.66 ± 36.02	301.66 ± 40.86	−9.81	0.0001**
Control	281.66 ± 36.62	295.66 ± 35.39	−10.01	0.0001**

$\overline{X}$, Mean; SD, standard deviation; *p*-value, level of significance.
** Significant.

types of exercise interventions, including running and resistance training. It was reported that loading stress can improve structural properties of bones and hence, it can enhance bone formation. Strains on bone greater than needed for steady state remodeling will cause a modeling response that increases bone mass to meet the increasing load requirement. This adaptive response occurs primarily during periods of growth and development denoting the importance of weight bearing exercises in children [34]. Also, bones become strengthened in response to loading as chemical composition of bones can be influenced by the degree and intensity of exercises [35]. Also, Joo et al. [36] showed that running exercise significantly increased BMD, bone volume, bone volume fraction, trabecular thickness and trabecular number.

Resistance and aerobic training provide exercising with weight bearing, this weight bearing provides stress on bone that in turn results in increasing bone strength and BMD. These results were consistent with Bradney et al. [37] and Welton et al. [38] who reported that weight bearing exercises are critical to ensure adequate bone mass formation in childhood and may be even more important than dietary calcium intake. The exact mechanism by which weight bearing exercises increase bone mass is related to dynamic strains in bone tissue regulating bone formation and resorption. High strains and high strain rates usually have osteogenic effect [39]. The skeleton is particularly responsive to the effects of weight bearing exercises during childhood, specifically during the pre-pubertal years [40]. Also, both muscle strength and bone mass can be improved by weight bearing exercises [41–43]. Ultimately, weight bearing exercises increase loading on bone which is most important in acquiring adequate bone mass in childhood than non-weight bearing exercises [44].

The results of this study also revealed that there was a significant improvement in muscle strength of knee flexors and extensors in the study group compared with the control group. This can be attributed to the combined effect of loading and resistance exercises that overload lower limb muscles. These results came in agreement with Hilberg et al. [10] who performed an experimental exercise protocol on 9 patients with hemophilia who participated in a 6-month specialized training program including gentle strength training with low resistance. There were significant improvements in isometric muscle strength and proprioceptive performance. Also, Pelletier et al. [45] found strength gains after a 3-week isometric exercise program in a single 12-year old participant.

These results also, point attention to the positive effect when combining resistance and aerobic exercise training in the form of treadmill and bicycle training that are performed in the present study. Visser [46] and Olama [47] showed that treadmill training is more effective than regular physical therapy program in increasing muscle strength and walking velocity. Treadmill training creates an environment that prevents the development of compensatory strategies compared with conventional gait training program. Also, Schonau et al. [48] reported a direct relationship between muscle strength and BMD suggesting that muscular strength can affect bone properties, including bone strength.

In the present study, it was observed that applying resistance exercises had a significant effect on knee flexors and extensors strength and this came in agreement with Elisa et al. [49] who reported the same results but on older women.

When comparing pre and post-treatment results of the 6MWT of both groups, it was observed that functional ability level of children with hemophilia in both groups was improved. These results were consistent with the findings of the American Thoracic Society (ATS) which emphasized that several factors may be contributed to functional improvement as increased stride length because of improved ROM; improved muscular endurance; improved cardiopulmonary efficiency; improved circulation; and improved biomechanical loading on the joints as a result of increasing ROM and muscle strength, resulting in a more comfortable and efficient gait. Behavioral and psychological factors such as increased confidence, improved body image, and decreased fear of movement or injury could also result in improvement in functional walking [15,23].

5. Conclusion

It can be concluded based on the obtained results that resistance and aerobic exercise training are effective in increasing

BMD and improving both muscle strength and functional ability in children with hemophilia.

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