

Incorporation of Pilates-based core strengthening exercises into the rehabilitation protocol for adolescents with patellofemoral pain syndrome: a randomized clinical trial

A.R. AZAB^{1,2}, W.K. ABDELBASSET^{1,3}, M.A. BASHA^{4,5}, W.S. MAHMOUD^{1,6},
A.E. ELSAYED^{7,8}, A.K. SALEH^{9,10}, R.K. ELNAGGAR^{1,2}

¹Department of Physical Therapy and Health Rehabilitation, College of Applied Medical Sciences, Prince Sattam bin Abdulaziz University, Al-Kharj, Saudi Arabia

²Department of Physical Therapy for Pediatrics, Faculty of Physical Therapy, Cairo University, Giza, Egypt

³Department of Physical Therapy, Kasr Al-Aini Hospital, Cairo University, Giza, Egypt

⁴Department of Physical Therapy, College of Medical Rehabilitation, Qassim University, Buraidah, Qassim, Saudi Arabia

⁵Department of Physical Therapy, ElSahel Teaching Hospital, General Organization for Teaching Hospitals and Institutes, Cairo, Egypt

⁶Department of Basic Sciences, Faculty of Physical Therapy, Cairo University, Giza, Egypt

⁷Pediatric Department, College of Medicine, Prince Sattam Bin Abdulaziz University, Al-Kharj, Saudi Arabia

⁸Pediatric Department, Faculty of Medicine, Alazhar University, Assiut, Egypt

⁹Surgery Department, College of Medicine, Prince Sattam Bin Abdulaziz University, Al-Kharj, Riyadh, Saudi Arabia

¹⁰Orthopedic Department, Faculty of Medicine for Girls, Alazhar University, Cairo, Egypt

Abstract. – OBJECTIVE: The objective of this study was to evaluate how a Pilates-based core strengthening exercise program affected pain, lower limb muscle strength, functional status, and health-related quality of life in adolescents with patellofemoral pain syndrome (PFPS).

MATERIALS AND METHODS: In this randomized controlled clinical trial, 34 teenagers with PFPS (ages 14-17) were randomly assigned to receive either a standard PT program (control group) or Pilates exercises plus the conventional program (study group). Both groups continued the treatment sessions for 3 months (3 sessions/week). Pain intensity, lower limb muscle strength (hip abductors and external rotators and knee extensors), functional status, and health-related quality of life were evaluated pre-and post-intervention.

RESULTS: Pain intensity ($p = .005$) reduced significantly post-treatment in the study group as compared to the control group, when controlled for the pre-treatment value. Also, muscle strength of hip abductors ($p = .002$) external rotators ($p < .001$), knee extensors ($p = .013$), functional status ($p = .002$), and health related quality of life ($p < .001$) increased significantly in the study group when compared to the control group.

CONCLUSIONS: The results of this study show that Pilates-based core strengthening exercises can help adolescents with PFPS reduce pain, enhance muscle strength, and improve their functional status and quality of life.

Key Words:

Pilates exercises, Functional status, Patellofemoral pain syndrome.

Introduction

One of the most frequent musculoskeletal pain problems is patellofemoral pain syndrome (PFPS) that tends to become a chronic problem¹. PFPS is common among young adolescents, particularly in physically active individuals aged 12 to 17 years old² with more prevalence among females, as it affects females 1.5-3 times when compared to males³. Retro-patellar (behind of kneecap) or peripatellar (around the kneecap) pain are common complaints among adolescents

with PFPS and crepitation in the knee joint, and also sitting with knee flexed for an extended period of time causes discomfort. Weight-bearing exercises, squatting, walking up or down stairs, and running are all known to aggravate symptoms by increasing the load on the patellofemoral joints⁴.

PFPS takes place whenever the muscles around the knee fail to keep the kneecap properly aligned, leading to abnormal lateral tracking of the patella⁵. Overuse, such as running and jumping sports, the trauma of kneecaps such as fracture, dislocation, or knee surgery may also predispose to PFPS⁶. Also, hip muscles weakness, especially abductors and external rotators of the hip could result in patellofemoral mal-alignment and development of PFPS⁷. During dynamic weight-bearing exercises, this weakness promotes femoral adduction and internal rotation, which increases the lateral patellofemoral joint vector and patellar tracking laterally as the femur rotates medially under the patella⁸.

Quality of life is a wide range concept with multi-dimensions which are physical, psychological, social, and personal. According to a recent study, PFPS predominantly affects young individuals and impacts on quality of life as severe medical conditions⁹. Silva et al¹⁰ also found a substantial decrease in quality of life in patients with PFPS, regardless of their athletic status, indicating that PFP has negative consequences on both adolescents' psychological and physical health.

Physical therapy plays a crucial role as a conservative treatment of PFPS; the treatment usually focuses on pain control and muscle strengthening¹¹. Currently, in patients with PFPS, exercise therapy has been shown to be useful in lowering discomfort and promoting strength; usually, it focuses on quadriceps strength and vastus medialis obliquus¹². Hip-strengthening activities should also be recommended in patients with PFPS in attempt to lessen pain and improve functional status¹³. Pilates exercise is an approach that uses body-mind-spirit interaction and concentrates on improving stability, muscle control, muscle strength, flexibility, breathing, and posture¹⁴. During the practice of Pilates exercise, a person has to exert mental effort and concentrate on the activation of certain muscles in functional sequences at a controlled speed¹⁵. Athletes have used Pilates to improve functional fitness. Also, it has been used by persons with medical problems like low back pain and knee arthritis to improve strength, balance, and flexibility¹⁶.

Since many prior studies have shown that Pilates training improves muscular strength/endurance, flexibility, and other clinical outcomes¹⁷, experimental research on its efficacy in adolescents with PFPS is inadequate. As a result, the focus of this research was to evaluate how pain, lower limb muscular strength, functional status, and quality of life changed following 12 weeks of Pilates-based core strengthening exercises in adolescents with PFPS.

Materials and Methods

Study Design

This was a randomized, controlled clinical trial conducted between November 2020 and August 2021. It was held at the College of Applied Medical Sciences' outpatient clinic at Prince Sattam bin Abdulaziz University (PSAU) in Saudi Arabia. PSAU's Physical Therapy Research Ethics Committee (No. RHPT/20/0049) granted ethical approval. All procedures were in accordance with the ethical standards of the 1975 Declaration of Helsinki. Participants and their guardians were instructed about the details of study procedures before the enrollment, and consent form was requested from them. The following identifier has been assigned to the study on ClinicalTrials.gov: NCT05120583.

An independent researcher who was uninformed of the treatment allocation assessed pain, lower limb muscle strength, functional status, and quality of life before and after the intervention.

Participants

Participants with PFPS were recruited from PT and orthopedic clinic where they attend for rehabilitation according to the following criteria: patients of both sexes, age ranged from 14-17 years, pain felt anterior to knee joint or retro-patellar during rest and increased with activities like prolonged sitting, squatting, running, and stair climbing. Insidious onset lasting for more than 6 weeks without any traumatic incidence, and not participating in a physical therapy program for the past three months. Subjects were excluded if they had a meniscal tear, cruciate/collateral ligaments involvement, knee osteoarthritis or rheumatoid arthritis, and if they had a previous patellar dislocation/subluxation, knee or hip surgery, traction apophysitis encompassing the patellofemoral complex, any pathology in the patellar tendon, or spinal referred pain.

Assignment Procedure

Thirty-four participants met the inclusion criteria. Following the baseline screening, they were divided into two equal-sized groups randomly. The control group ($n = 17$) received the traditional physical therapy (TPT), and the study group ($n = 17$) received Pilates exercises in addition to the TPT program. An independent researcher used a basic randomization approach in which she drew sealed non-transparent envelopes with a code for one of the two experimental groups (control or study).

Outcome Measures

An independent investigator who was unaware of the group intervention measured pain, lower limb muscle strength, functional status, and quality of life before and after intervention.

Primary Outcome Measures

Pain Assessment

Pain degree was assessed by using a visual analog scale (VAS), 10-cm VAS scale, with 0 indicating no pain and 10 for worst pain sensation. Participants were asked to bisect the line at a point representing the degree of pain they perceived at rest and/or during activity¹⁸.

Muscle Strength Assessment

The maximum voluntary isometric muscle strength of hip abductors, external rotators and knee extensors was assessed using a calibrated handheld dynamometer (Micro FET2, Hoggan Health Technologies Inc., UT, USA). A demonstration session was dedicated to all participants for familiarizing them with the assessment procedures. Each participant was encouraged to exert as maximum effort as possible. For each muscle group, three 5-second contractions were performed, and the average score (in newtons) was calculated and adopted for the analysis. The participant position and dynamometer placement were as follow.

For the hip abductors, participants assumed a supine position with the untested limb in flexion knee position to decrease stress on low back muscles and the tested limb in full extension with 10° abduction hip, the therapist stood beside the tested limb with one hand supporting the participant's pelvis and the other holding the dynamometer lateral to the knee joint to resist hip abduction. Participants were in a prone position

for hip external rotators, with the tested limb at 90° flexion knee while the therapist stood on the opposite side of the tested limb, holding the dynamometer in one hand dynamometer just proximal to medial malleolus to resist hip external rotation and supporting the participant's pelvis with the other.

Participants sat in a chair with their hips and knees bent at 90° for knee extensors, while the therapist stood beside the tested limb. The handheld dynamometer was aligned with the midpoint of the ankle joint on the anterior aspect of the leg, just superior to the lateral malleolus to resist the knee extension.

Secondary Outcome Measures

Functional Status

Functional status was evaluated using the Arabic version of the Anterior Knee pain Questionnaire (Kujala Questionnaire)¹⁹. It is a self-reported 13-item questionnaire that assesses the functional limitations caused by patellofemoral pain. These questions report pain, abnormal patellar movement, swelling, knee flexion limitation and quadriceps muscle atrophy during six physical activities that are walking, sitting, squatting, stairs climbing, jumping and running. The score goes from 0 to 100, with 0 suggesting full functional impairment and 100 denoting no pain or functional restriction. The scale has a moderate validity and a high test-retest reliability ICC = .86-.94²⁰.

Quality of Life

The quality of life was evaluated using the self-report Pediatric Quality of Life Inventory (PedsQL). PedsQL is a multidimensional assessment of children's and adolescents' health-related quality of life (HRQL); it includes 23 items distributed among 4 domains [physical (8 items), emotional (5 items), social (5 items), and school functions (3 items)]. This questionnaire has been approved for use with children and adolescents aged 2 to 18 years²¹. Each item is rated on a 5-points scale (0 means never, and 4 means almost always). Items are transformed linearly to 0-100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0). For this study, we calculated the physical health summary score (sum of item scores in the physical domain divided by the number of rated items), psychosocial health summary score (sum item

scores of the emotional, social, and school functions domains divided by the number of rated items), and the total summary score (the sum of all item scores divided by the number of rated items in all domains). Higher values indicate better quality of life.

Intervention

Traditional Physical Therapy Program (TPT)

Participants in both groups received the TPT program (60 minutes/session, three sessions per week for three months). The aim of the program was mainly to relieve pain, improve muscle strength, increase flexibility, and promote functional status. Electrotherapy (ultrasound and infrared), stretching of the muscles surrounding the hip and knee, and strengthening of the muscles around the hip and knee are all part of the program^{22,23}.

Pilates Exercises

Patients in the study group received Pilates exercises (25 minutes/ session). There are different types of equipment to be used in Pilates exercises to achieve different purposes; mat, Pilates band or elastic bands, and Pilate's ball were used (Table I)²⁴.

Power Analysis and Sample Size

To draw an accurate conclusion about the intervention effect, a preliminary power analysis was carried out through the G-power software (version 3.1.9.2, Dusseldorf, Germany) to identify the appropriate sample size. Predicated on estimates of means ($M1 = 6.1$ and $M2 = 4.2$) of pain intensity (VAS score), which were collected from a small pilot study including eight children with PFPS who were undertaken similar interventions, a total sample of 28 subjects (i.e., 14 per group) was required to achieve a power of 90% to detect the difference between groups, in an ANCOVA study, with an alpha level of .05. The covariate had a coefficient of determination of 0.324. The effect size was represented by their standard deviation which was 0.95. The common standard deviation within a group was assumed to be 1.80. To account for the possible dropouts (~ 20%), the sample size increased to 34 subjects (17 per group).

Statistical Analysis

All statistical analyses were performed using SPSS software, Version 26 for Windows (SPSS Inc., Armonk, NY, USA). The hypothesis that data comes from a normal distribution was tested through the Shapiro Wilk test. The intention-to-treat analysis was applied for the between-group comparison. Stochastic regression imputation was employed to replace missing data with substituted values. The between-group difference regarding primary and secondary outcome measures post-treatment was computed through analysis of covariance (ANCOVA) test, where the pre-treatment scores of each variable were used as covariates for assessing the difference between study and control groups. When the ANCOVA analysis indicated a difference, the effect size was calculated through the partial eta-squared (η^2_p) formula. For all statistical tests, the α -level for determining statistical significance was $p < 0.05$.

Results

Recruitment and Retention of Participants

Figure 1 shows the CONSORT flow diagram for enrollment, randomization and retention of the study participants. Out of 52 potentially eligible adolescents, 34 participants fulfilled the inclusion criteria and were randomly allocated to either of the control or the study group. Three participants [two from the control group and one from the study group] were did not complete the study because they either moved away from the working or had a scheduling issue. However, their data were included in the analysis per the intention-to-treat principle.

Baseline Demographic Data

Table II summarizes the study participants' baseline demographic and clinical characteristics. All anthropometric and demographic variables (i.e., age, weight, height, and body mass index) were comparable between the control and study groups ($p > .05$). The PFPS-related clinical characteristics like pain duration and number of participants who regularly use pain killers, and the frequency of engagement in sports activities per were also equivalent in both groups ($p > .05$).

Table I. Pilates exercises (adopted from²⁴⁻²⁵).

Exercise	Exercise description	Equipment used	Repetitions x sets
Stage 1 for 4 weeks			
Mat exercises Hundred exercise	Participants were supine lying with hips and knees were flexed 90° degrees, and the shin of the tibia was parallel to the ground; participants were instructed to take deep breath and contract abdominal muscle then exhale while raising their head, up curl their shoulder up of the floor, then extend their arms straight and low just a few inches away from the floor, and move arms in a controlled up and down manner for 100 counts.	Mat	5 × 3
Single leg stretch	Participants were supine lying with hips and knees were flexed 90° degrees, and the shin of the tibia was parallel to the ground, breathe in, then breathe out while raising their head up, curl their shoulder up of the floor then, breathe in and bring left knee to chest while stretching the right, then change. Pulling knees should be in unison with breathing	Mat	5 × 3
Plank	The participant had both upper arms parallel to his elbows and shoulders width apart, with both knees were in full extension and toes pointed in planter-flexion, the participant was instructed to maintain head, trunk and lower limbs in straight position. Then breath in and breathe out and abduct hip for 30 degrees	Mat	5 × 3
Standing footwork	Patient was in standing position in “V stance” While keeping the Pilates “V”, the patients were instructed to rise up on their toes as far as possible while keeping the heels together. Then they lowered to the ground while keeping their spine neutral. Then the patient was instructed to perform a plié (bending at the hips and knees). The patient was instructed to breathe in deeply after beginning the movement and breathe out when performing the movement.	Mat	5 × 3
Stage 2 for 4 weeks using elastic band (Pilates band)			
Hip twist	Participants were supine lying position with both knees were bent and elastic band around the knees, breathe in deeply and breathe out while abducting both lower limbs. Then move both feet up so lower limbs become in right angles hip and knees, then inhale and exhale while abducting both lower limbs	Pilates band	
Side kick internal/external rotation with Pilates band	While children lying on their right side with hip flexed approximately 45 degrees with elastic resistance strap surround the knee (Pilates band), breathe in deeply and breathe out while abducting and rotating out the upper leg, then slowly lowers the leg, and then repeat the sequences on the left side.	Pilates band	8 × 3
Squat	Patient was in standing position with both feet on the Pilates band and hold onto both ends with his/her hands and elbows straight. Take deep breath then breathe out. Squat and bend knees to 90 degrees and elbows to 90 degrees, then stand back up	Pilates band	8 × 3
Stage 3 for 4 weeks using ball			
Swimming with stabilization ball	Participants were in prone position while holding a Pilates ball with out-stretched hands, lower limbs in slight abduction. Inhale while moving the upper limbs up and move lower limbs up and down reciprocally, then exhale while moving the upper limbs down and lower limbs still moving up and down reciprocally.	Pilates ball	10 × 3
Wall squat rolls	Patient stands against a wall with a Pilates ball in the middle of the back. The distance between the feet and the wall should be around a foot. Slowly lower yourself onto the ball to a squat position, keeping knees from going past ankles. Recover balance by slowly rolling back up. That counts as one rep.	Pilates ball	10 × 3

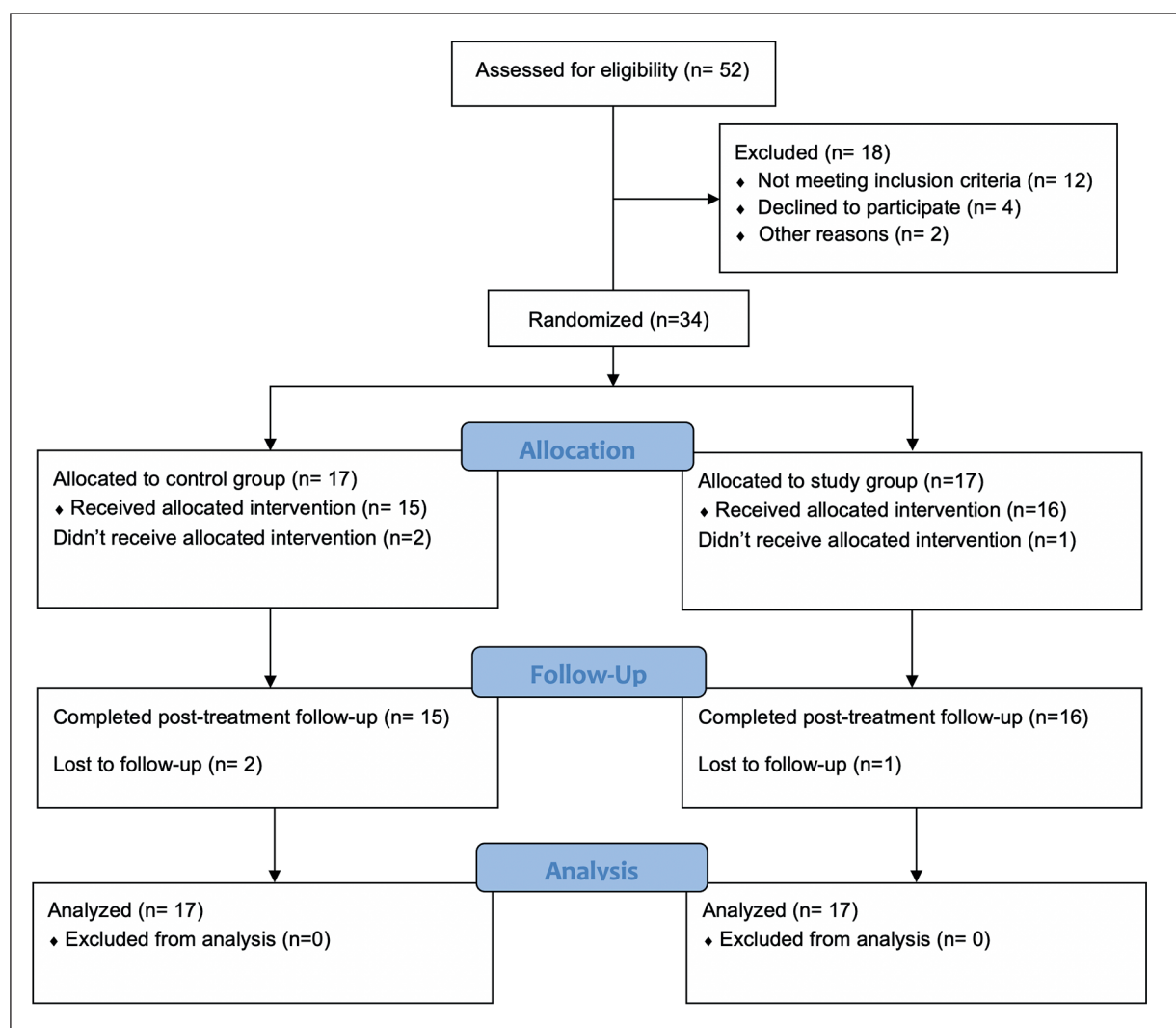


Figure 1. Participants' flowchart.

Table II. Clinical and demographic profiles of participants at the beginning of the study.

	Control group (n = 17)	Study group (n = 17)	p-value
Age, year	15.18 ± 1.13	15.65 ± 1.11	.23 [†]
Gender (boys/girls), n (%)	5 (29.4)/12 (70.6)	7 (41.2)/10 (58.8)	.72 [‡]
Weight, Kg	50.47 ± 7.86	54.35 ± 5.63	.11 [†]
Height, m	1.52 ± 0.10	1.56 ± 0.07	.15 [†]
BMI, Kg/m ²	21.76 ± 1.32	22.13 ± 1.21	.41 [†]
Pain duration, months	26.18 ± 6.73	23.12 ± 5.84	.17 [†]
Regular use of pain killers, (yes/no) n (%)	6 (35.3)/11 (64.7)	3 (17.6)/14 (82.4)	.43 [‡]
Sports participation, times/week	3 (2-4)	2 (1-4)	.29 [§]

Continuous data expressed as mean ± SD and categorical data shown as frequency (%), and sport participation data are listed as median (min-max). Abbreviations: BMI: body mass index, [†]Independent t-test, [‡]Fishers' exact test, [§]Mann Whitney U test.

Difference Between Groups

The pre-to-post change differences between the control and study groups are demonstrated in Table III. According to the ANCOVA analysis, there was a significant large post-treatment difference between the control and study groups in pain intensity [$F_{(1, 31)} = 9.14, p = .005, \eta^2_p = 0.23$] when controlled for the pre-treatment values, in favor of the study group. Likewise, the analysis demonstrated significant differences among both groups regarding strength of hip abductor muscles [$F_{(1, 31)} = 11.18, p = .002, \eta^2_p = 0.26$], hip external rotator muscles [$F_{(1, 31)} = 31.64, p < .001, \eta^2_p = 0.51$], and knee extensor muscles [$F_{(1, 31)} = 6.94, p = .013, \eta^2_p = 0.18$], where strength changes from the pre-to post-treatment occasion in the study group were more favorable when compared to that of the control group.

Similar trends were also observed regarding changes in the secondary outcomes. There was a significant post-treatment difference between control and study groups in functional status [$F_{(1, 31)} = 11.59, p = .002, \eta^2_p = 0.27$] favoring the study group, with controlling for the pre-treatment scores. In addition, a significant post-treatment differences were observed between both groups with respect to quality of life; physical health [$F_{(1, 31)} = 7.71, p = .009, \eta^2_p = 0.19$], psychosocial health [$F_{(1, 31)} = 5.03, p = .032, \eta^2_p = 0.14$], and total quality of life score [$F_{(1, 31)} = 13.81, p < .001, \eta^2_p = 0.31$] as controlled for the pre-treatment scores of each variable, where participants in the study group reported better quality of life scores.

Discussion

PFPS is among the most frequent musculoskeletal symptoms among adolescents, and it impacts many activities of regular activities, including running, climbing stairs, kneeling, and squatting, leading them to be less active than their peers of the same age²⁶. The goal of this study was to see how 12 weeks of Pilates exercises made an impact besides conventional physical therapy on pain, lower limb muscles strength, functional status, and quality of life in adolescents with PFPS. This study's findings revealed that incorporation of Pilates exercises to the conventional physical therapy program induces a more favorable reduction in pain intensity and improves muscular strength, functional status, and quality of life in comparison with conventional physical therapy in isolation.

Isometric exercises have been found to be useful in the treatment of various knee issues, and certain Pilates exercises, such as the hundred and single-leg circle, incorporate specific components of isometric exercises. Lange et al²⁷ found that in 50-70% of individuals with knee osteoarthritis, isometric muscular contraction in Pilates activities can reduce discomfort and improve function. A study was also conducted by Chang et al²⁸, on 41 women with mild to moderate osteoarthritis of the knee, compare between resistance using elastic Thera- band and conventional exercises. Moreover, they found that 8 weeks of resistance exercises by using elastic Thera-bands

Table III. Overview of ANCOVA analysis (post-treatment differences between study groups regarding dependent variables, controlled for the pre-treatment scores).

Variables	Pre-treatment		Post-treatment		Pre-to-post change difference	
	Control	Study	Control	Study	p-value	η^2_p
Pain intensity VAS	7 (5-8)	7 (5-9)	5 (4-6)	4 (2-6)	.005*	0.23
Muscle strength (in Newton)						
Hip abd.	44.64 ± 7.83	45.98 ± 8.21	45.81 ± 7.31	50.80 ± 6.62	.002*	0.26
Hip ext. rot.	33.24 ± 3.13	36.46 ± 5.70	34.32 ± 2.49	42.43 ± 6.13	< .001*	0.51
Knee ext.	59.10 ± 7.55	59.85 ± 8.69	61.20 ± 5.83	65.52 ± 6.96	.013*	0.18
Functional capacity ANPQ	68.33 ± 11.94	67.86 ± 12.34	71.19 ± 8.65	75.49 ± 11.49	.002*	0.27
Quality of life						
Physical	84.46 ± 6.47	81.14 ± 7.61	86.48 ± 3.69	91.41 ± 5.90	.009*	0.19
Psychosocial	77.63 ± 5.38	80.40 ± 4.88	85.38 ± 4.79	90.45 ± 5.71	.032*	0.14
Total score	81.04 ± 4.40	80.78 ± 3.56	85.93 ± 2.78	90.93 ± 4.56	< .001*	0.31

Data expressed as mean ± standard deviation except pain intensity listed as median (min-max). Abbreviations: VAS: visual analogue scale, abd: abductor muscles, ext. rot.: external rotator muscles, ext.: extensor muscles, ANPQ: anterior knee pain questionnaire. *Significant at $p < 0.05, \eta^2_p$: the effect size for significant ANCOVA test.

with its four colors can significantly enhance lower-extremity function among females with mild-to-moderate knee OA.

Our result came in agreement with a study by Yazic and Mohammadi²⁹ on 11 young males with patellofemoral pain syndrome for ten weeks, who found significant improvement in Step-down, right and left single-leg press, daily activities, and functional performance after the Pilates exercises. Also, a comparative study by Akodu et al³⁰ on 33 participants with osteoarthritis of the knee found that Pilates exercises were more effective in lowering the severity of pain and functional limitations, as well as the range of motion of the knee than isometric exercises. Furthermore, Kalra et al²⁴ studied the impact of Pilates exercises on 40 young males (17-28 years) and reported that lower extremity strength, flexibility, dynamic balance, and coordination all improved significantly.

The role of Pilates in improving function may be due to the usage of apparatus (Pilates ball and Thera-band), it has been claimed to provide large sensory system stimulation, giving comprehensive feedback, promoting optimal performance³¹. It has also been suggested that such an improvement in functional status following Pilates training might be associated with the placebo effect inherent in the application of Pilates's equipment³².

The findings of the current study on Pilates' involvement in pain relief were consistent with those of a review study by Wells et al³³, which checked the data for the impact of Pilates exercises on chronic low back pain patients. This review study indicated that Pilates exercise improves pain and functional ability more than traditional physical activity. Pain reduction following Pilates training might be explained by relieving stress, as breathing exercise, which is essential in Pilates, encourages good circulation, improve lung capacity, improve oxygenation and help to trigger the mind to release endorphins, the natural 'feel-good' hormones and creates a physiological response in the body which decreases stress and pain³⁴. Another probable mechanism is increased flexibility. Segal et al³⁵ have demonstrated that Pilates exercises lead to increased flexibility, which promotes better physical performance and lowers the energy-cost of joint movement as a consequence of decreased muscle tension and reduced soreness injury during physical exercise.

Our results also indicated that 12 weeks of Pilates-based core strengthening exercises in ad-

olescents with PFPS improved their quality of life. Enhanced quality of life could have been associated with reduced pain perception and improved functional ability. This claim was based on the findings of a study conducted by van der Heijden et al³⁶, who claimed that exercise therapy improved pain relief, functional status, and long-term quality of life for PFPS patients. Moreover, Mendonça et al³⁷ found that Pilates-based core strengthening exercises had a considerable favorable impact on physical and mental components of health-related quality of life in patients with painful musculoskeletal conditions like juvenile idiopathic arthritis.

The findings of the study should be considered in light of some limitations. The major limitations of the current study were shortage of the long-term follow-up, sample size that is rather small, restriction of the sample to the adolescence stage. So, further studies that take the limitations mentioned above into account will need to be undertaken to reach a firm conclusion about the relevance of Pilates-based strengthening exercises in patients with PFPS.

Conclusions

Based on clinical findings of the present study, 12 weeks of Pilates training has the potential to alleviate pain, increase lower limb strength, enhance functional ability and promote quality of life when incorporated into the conventional physical therapy protocol more favorably than the conventional physical therapy alone. However, additional studies into the role of Pilates in the treatment of PFPS patients would help us to establish a greater degree of accuracy on this matter.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

Conception and design: Alshimaa Azab, Waleed Mahmoud, Ragab Elnaggar, Abbas Elsayed. Analysis and interpretation of data: Ragab Elnaggar, Ayman Saleh, Abbas Elsayed, Walid Abdelbasset. Drafting the article: Alshimaa Azab, Walid Abdelbasset, Maged Basha, Ayman Saleh, Waleed Mahmoud. Supervision: Alshimaa Azab, Ragab Elnaggar, Maged Basha. Validation and final approval of the version of the article to be published: Alshimaa Azab, Walid Abdelbasset, Maged Basha, Waleed Mahmoud, Abbas Elsayed, Ayman Saleh, Ragab Elnaggar.

ORCID ID

Alshimaa Azab: <https://orcid.org/0000-0002-9533-0699>;
Walid Abdelbasset: <https://orcid.org/0000-0003-4703-661X>;
Maged Basha: <https://orcid.org/0000-0002-3422-6193>;
Waleed Mahmoud: <https://orcid.org/0000-0002-8545-3433>;
Abbas Elsayed: <https://orcid.org/0000-0002-5633-1920>;
Ayman Saleh: <https://orcid.org/0000-0002-0296-5274>;
Ragab Elnaggar: <https://orcid.org/0000-0001-5080-702X>.

Data Availability Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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