



## Original Article

### Effects of Pulmonary Rehabilitation on Endurance and Quality of Life in Patients with Pulmonary Hypertension; A Randomized Controlled Trial

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#### ABSTRACT

**Background:** Pulmonary hypertension has been known as a rather serious condition as it affects the right side of the heart and eventually results in severe pulmonary conditions. The pulmonary arteries tend to become thick and inelastic. The functioning of the pulmonary system impairs and affects the oxygenation of the entire body. **Objective:** To determine the effects of pulmonary rehabilitation on endurance and quality of life in patients with pulmonary rehabilitation. **Methods:** Our current study is a randomized controlled trial. A purposive sampling technique was employed for sampling and 49 patients were randomly allocated into each group by lottery method. This trial was conducted at Bajwa Hospital, Shahdhrh, Lahore, Pakistan. The already diagnosed patients with pulmonary hypertension, employing World Health Organization with functional class II-IV were recruited in this study. The patients with heart failure NYHA class III and IV, mitral stenosis and systemic sclerosis were excluded from the study. The 6-minute walk test for endurance, Duke Activity Status Index for activity status and short form 36 for assessing quality of life were employed in the study. **Results:** The results of our study show that there is a significant difference between the groups pre and post-intervention. The majority of the data showed a p-value less than 0.05 so this indicates that data is not normally distributed and a non-parametric Mann-Whitney U test was applied between Groups 1 and 2 analysis for a 6-minute walk test. Both groups' baseline median for the 6-minute walk test had a p-value of 0.357 whereas for the 6-week median, the p-value was 0.000 which represents a statistical difference between the groups after the application of 6 weeks training program and medical treatment. Mann-Whitney U test was applied between Groups 1 and 2 analysis for Duke Activity Status Index score pre and post-intervention. **Conclusion:** This concluded that pulmonary rehabilitation significantly improves endurance, emotional well-being, general health, activity status and quality of life among patients with pulmonary hypertension.

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## INTRODUCTION

Numerous studies have recommended and suggested that quality of life and exercise capability tend to be reduced in patients with pulmonary hypertension. Several studies were conducted which prove that exercise-based rehabilitation programs bring enhancements in exercise capacity and quality of life in patients with pulmonary hypertension.<sup>1</sup> Pulmonary Hypertension is known as a severe clinical condition which is categorized by mean pulmonary pressure greater than 25 mm Hg at rest, an expiratory pulmonary artery wedge pressure less than or equal to 15 mm Hg and a pulmonary vascular resistance of greater than three wood units. Pulmonary Hypertension can be categorized into idiopathic arterial hypertension and pulmonary hypertension which is concomitant with congenital heart disease, systematic to pulmonary shunt, rheumatic diseases, portal hypertension and human immunodeficiency virus infection.<sup>2</sup> Patients with pulmonary hypertension tend to have reduced exercise capacity, general health, emotional well-being, quality of life and survival.<sup>3,4</sup> Various studies have recommended that exercise training programs might lead to benefiting patients with clinically stable chronic diseases, diseases in which patients have been diagnosed with heart failure are the chronic disease population that superlative recognizes the reimbursements of exercise training.<sup>5</sup>

The prognosis of pulmonary hypertension has been observed to greatly improve in the past twenty years due to advancements in the targeted drug therapy for the treatment of pulmonary hypertension. However, the overall long-term prognosis of pulmonary hypertension patients still vestiges substandard,<sup>6</sup> majority of the patients will pulmonary hypertension still have been observed to have impaired exercise capacity

and reduced survival levels.<sup>7</sup> In 2009 The European Society of Cardiology provided guidelines for diagnosing and treating pulmonary hypertension which suggested that patients with pulmonary hypertension must be encouraged to stay active within the limits of their symptoms.<sup>8</sup> This suggestion was based on the results of a randomized controlled trial that worked on observing the exercise capacity and quality of life in patients with pulmonary hypertension who participated in an exercise training plan and were compared with an untrained control group.<sup>9</sup> The advantageous effects of exercise rehabilitation training were represented majorly through an enhancement in the 6-minute walk test, peak oxygen uptake, hemodynamics, cardiorespiratory functioning, scoring for quality of life questionnaire, exercise capacity in various types of patients with pulmonary hypertension. Because of growing number of evidence, guidelines suggest that stable pulmonary hypertension patients must conduct a closely administered exercise and respiratory training program as an add-on therapy.<sup>10,11</sup>

The contrivances through which the exercise rehabilitation training marks the pulmonary hypertension are not entirely unblemished, they are vague hence a large number of clinical trials are needed to endorse its efficacy, effectiveness and safety. Furthermore, future researchers are suggested to conduct studies that would be interesting and would focus on investigating the effects of various types of training programs, for example, isometric strength training, which has recently been proven to be meaningfully different from endurance training within the milieu of physiological adaptations.<sup>12,13</sup> The already surviving literature seems to designate that exercise-based pulmonary rehabilitation training programs comprising of appropriate

intensity and frequency might be improving the prognosis and quality of life of patients with pulmonary hypertension. Notwithstanding these findings, the exercise-based rehabilitation training program in patients with pulmonary hypertension is still limited by numerous gaps in knowledge and literature regarding the optimal method of rehabilitation and the duration and intensity of the training program and its sessions. So, there should be conduction of studies systematically which compare the training modalities and intensities among various types of subgroups. Nevertheless, these findings also show us that the rehabilitation training programs should be regulated and conducted under the supervision of professional staff, and should also be provided with an adjunct therapy to the pharmacological treatment. The cardiac and pulmonary rehabilitation training program have become an integral and substantial part of wide-ranging treatment for coronary heart disease but is still being reconnoitered in the context of pulmonary hypertension. Our current study intends to fill this gap in the literature.<sup>13</sup>

The purpose of the current study was to evaluate the effects, efficiency and well-being of exercise-based rehabilitation programs in patients with pulmonary hypertension. Underdeveloped countries like Pakistan need more economic interventions for treating issues like pulmonary hypertension. It would add authentic and reliable literature regarding the positive effects of pulmonary rehabilitation for bringing improvements in the lives of patients with pulmonary hypertension. The current study worked on determining the effects of pulmonary rehabilitation exercise on patients with pulmonary hypertension under the supervision of a professional physiotherapist. This study would fill the gap considering the benefits of pulmonary

rehabilitation exercise programs on the Pakistani population.

## METHODS

This current study is a randomized controlled Trial (pre and post-test control group design). The purposive sampling technique<sup>14</sup> was employed for sampling the participants into two groups and then were randomly allocated into groups by lottery method.<sup>15</sup> The data for our current study was collected from Bajwa Hospital, Shahdrah, Lahore, Pakistan. The sample size was calculated using the online epitool app and was calculated to be 98.<sup>16</sup> 98 patients with already diagnosed pulmonary hypertension were recruited in our study. The inclusion criteria of our current study were, already diagnosed patients with pulmonary hypertension, World Health Organization (WHO) with functional class II-IV.

The age range was considered to be 18 to 80 years. Patients were required to be stable and compensated with ideal medical therapy (iloprost, endothelin antagonists, sildenafil, anticoagulants, diuretics and supplemental oxygen) for at least three months before entering our current study.<sup>1</sup> The recruited population of selected patients who fulfilled the inclusion criteria were allocated to two groups, Group A (experimental group) and Group B (control group). After the allocation, the consent forms both in English and Urdu were given to every participant. The patients in the experimental group received exercise programs considering, walking, low-load cycling, stretching and breathing techniques i.e. pursed lip breathing and muscle training along with optimized medication therapy under the supervision of a respiratory physiotherapist for six weeks. Participants were also asked not to perform any extensive exercise program on their own. The patients in both groups were also encouraged to perform

activities of daily living regularly. This six-week pulmonary rehabilitation program was planned to improve exercise capacity and health status. This experimental group will also be receiving the optimized drug therapy. The patients in the control group received conventional therapy for six weeks along with optimized drug therapy (iloprost, endothelin antagonist, sildenafil, calcium channel blockers anticoagulants, diuretics and supplemental oxygen).<sup>1</sup> The tools employed in our current study were a 6-minute walk test, spirometry test, VO<sub>2</sub> maximum, echocardiography and SF 36. Scoring of the outcomes measures was performed at the baseline and after 6 weeks of receiving the interventions. For the experimental group, the heart rate and oxygen saturation were monitored continuously throughout the training and were employed to adjust the intensity of the training (Progression).

When the oxygen saturation level of a patient was reduced to 85% the training was reduced. Approval was taken before starting this study from the ethical committee of Riphah International University, Pakistan. Informed and written consent was taken from all the participants about the procedure and interventions employed in this study. All the necessary precautionary measures were taken and surety was affirmed that no physical or emotional harm would happen to any participant. Confidentiality of the patients was assured to be maintained.

Details of the 6-Week Pulmonary Rehabilitation Plan:

#### **Week 1: (Alternative days)**

Low-load cycling; Bicycle ergometer training with a lower workload (10 to 30 W)  
Walking: five minutes on flat ground  
Stretching five repetitions  
Breathing technique (pursed lip breathing)

five repetitions

#### **Week 2: (Alternative days)**

Bicycle ergometer training with a lower workload to a higher workload of 20 to 60 W for 10 to 25 minutes per day progressively, maximum ranging from 60% to 80% of the heart rate

Walking: 10 to 15 minutes on flat ground

Stretching five repetitions

Breathing technique (pursed lip breathing) five repetitions

#### **Second to Sixth Week: (Twice a week)**

Stretching five repetitions

Breathing technique (pursed lip breathing) five repetitions

Resistive muscle training: training employing the usage of equipment like a dumbbell of the muscles of the upper limb with lesser heavy objects (500g to 1000g).<sup>1</sup>

This 6-minute walk test is a sub-maximal exercise test which is employed to check the aerobic activity and endurance of the patients.<sup>17</sup> The spirometry test was employed in our study to measure the breath. It was employed for checking the functioning of the lung with its measurements especially inhalation and exhalation of the breathing, speed and volume.<sup>18</sup> Duke Activity Status Index was also employed in our current study to examine the functional capacity of the patients. It was employed to check the effects of medical treatment and the pulmonary rehabilitation plan with a score that ranges from 0 to 58.2. Higher scores indicate a higher functional capacity.<sup>19</sup> Echocardiography was also employed in our current study. It is the ultrasound of the heart which tends to explain the enlargement of the right chamber of the heart with thickened intra-ventricular septum in patients suffering from pulmonary hypertension. It also aims to measure the structural imaging recruited in our study pre and post-test was checked by

**Table 1:** Normality of Variables and Their P-values (Using Shapiro-Wilk Test)

Variables	Follow-up	Group 1 p-value	Group 2 p-value
<b>6 MWD</b>	Baseline	0.052	0.028
	6 weeks	0.005	0.932
<b>DASI Score</b>	Baseline	0.006	0.008
	6 weeks	0.003	0.004
<b>Physical function</b>	Baseline	0.014	0.326
	6 weeks	0.007	0.211
<b>Role limitations due to physical health</b>	Baseline	0.019	0.021
	6 weeks	0.003	0.116
<b>Energy /fatigue</b>	Baseline	0.024	0.030
	6 weeks	0.002	0.010
<b>Social functioning</b>	Baseline	0.007	0.149
	6 weeks	0.027	0.138
<b>Pain</b>	Baseline	0.054	0.015
	6 weeks	0.001	0.008
<b>Role limitations due to emotional problems</b>	Baseline	0.043	0.006
	6 weeks	0.030	0.009
<b>Emotional well-being</b>	Baseline	0.018	0.107
	6 weeks	0.055	0.021
<b>General Health</b>	Baseline	0.009	0.007
	6 weeks	0.004	0.010
<b>FEV1</b>	Baseline	0.005	0.000
	6 weeks	0.003	0.415
<b>FVC</b>	Baseline	0.279	0.042
	6 weeks	0.062	0.159
<b>PEF</b>	Baseline	0.348	0.080
	6 weeks	0.251	0.10

employing SF-36. It consists of 36 items and eight sub-scales which cover the domains of physical functioning, body pain, vitality,

general health, emotional and mental health and social functioning. The higher the score the less would be the disability or a higher level of

quality of life. This scale also evaluates the health status of the patient and the cost-effectiveness of the treatment and monitors and compares the burden of the disease.<sup>21</sup> All these tools were used to measure the outcome scores pre and post-test within and between groups. All the collected data was put and analyzed using Statistical Package for Social Sciences (SPSS) Version 23. The normality of all the variables was tested by employing Shapiro Wilk test. Mann-Whitney test was employed for between-group analysis. Results were represented in the form of tables and graphs.

**RESULTS**

Table 1 represents the normality of the variables. The majority of the data shows a p-value less than 0.05 so this indicates that data is not normally distributed so the test of choice is non-parametric. Table 2 represents the statistical distribution of the gender in this current study. Table 3 represents the result of the Mann-Whitney U test applied between Group 1 and 2 analysis for the 6-minute walk test pre and post-test. Group 1 and 2 baseline median for 6 minutes walk test had p- a value of 0.357 whereas for the 6-week median the p- value was 0.000 which represents a statistical difference between the groups after the application of 6 weeks of training program and medical treatment. Table 4 represents the

**Table 2: Statistical Distribution of Gender**

Gender	Group 1 f (%)	Group 2 f (%)
Male	17 (34.7%)	18 (36.7%)
Female	32 (65.3%)	31 (63.3%)

Mann-Whitney test applied for between Group 1 and 2 analysis for DASI score pre and post-intervention. The p-value came out to be 0.000 which shows the statistical difference between the groups after the 6-week training program.

Table V represents the Mann-Whitney U test applied between groups 1 and 2 analysis of general health pre and post-intervention. Table 4 represents the Mann-Whitney U test applied between Group 1 and 2 analysis of emotional well-being pre and post-intervention.

**Table 3: Mann-Whitney U test for between Group 1 and 2 Analysis of 6 Minute Walk Distance Pre and Post-Intervention**

6MWD	Group Median (IQR)	Group 2 Median (IQR)	Mann Whitney U test (p-value)
Baseline	401 (28)	398 (28)	0.357
Post 6 Weeks	432 (51)	408 (18.5)	0.000

**Table 4: Mann-Whitney U test applied for between Group 1 and 2 Analysis of DASI Score Pre and Post-Intervention**

DASI Score	Group1 Median (IQR)	Group 2 Median (IQR)	Mann Whitney U test (p-value)
Baseline	25 (3)	25 (3.5)	0.620
Post 6 Weeks	36 (8)	27 (6)	0.000

**DISCUSSION**

The results of our study show us that there is a significant difference between the groups pre and post-intervention. The majority of the data shows a p-value less than 0.05 so this indicates that data is not normally distributed so the test of choice is non-parametric. The Mann-Whitney U test was applied between Group 1 and 2 analysis for the 6-minute walk test pre and post-test. Group 1 and 2 baseline median for 6 minutes walk test had a p-value of 0.357 whereas for the 6-week median, the p-value was 0.000 which represents a statistical difference between the groups after the application of the 6-week training program and medical treatment.

**Table 5: Mann-Whitney U test for between Group 1 and 2 Analysis of General Health Pre and Post-Intervention**

SF36 (General Health)	Group 1 Median (IQR)	Group 2 Median (IQR)	Mann Whitney U test (p-value)
Baseline	48(25)	51(24)	0.577
Post 6 Weeks	77(13.5)	54(22)	0.000

**Table 6: Mann-Whitney test applied between Group 1 and 2 Analysis of Emotional well-being Pre and Post-Intervention**

SF36 (Emotional well-being)	Group 1 Median (IQR)	Group 2 Median (IQR)	Mann Whitney U test (P Value)
Baseline	51(10)	51(9)	0.583
Post 6 Weeks	61(16.5)	55(11.5)	0.000

The Mann-Whitney U test was applied between Group 1 and 2 analysis for DASI score pre and post-intervention. The p-value came out to be 0.000 which shows statistical difference between the groups after the 6-week training program. Xiamomei Zeng and co-workers conducted a study to determine the effects and welfare of exercise training and rehabilitation in pulmonary hypertension.

Their results conclude that exercise training has been perceived to be associated with noteworthy improvement in exercise capacity, cardiorespiratory fitness and quality of life among patients with pulmonary hypertension and it proved to be safe for stable patients with pulmonary hypertension with optimization and medical therapy.<sup>22</sup> Our current study agrees with the conclusion made by them. However, our current study and their study suggested and recommended that more large-scale multicenter studies are needed to be conducted

to confirm the efficacy, effectiveness and safety of exercise training in patients with pulmonary hypertension. Goksen Kuran Aslan and co-workers conducted a randomized controlled trial to determine the effects of inspiratory muscle training in pulmonary hypertension. They focused on determining their effects on respiratory functions, physical activity, functional exercise capacity and quality of life. The results of their study demonstrated that threshold inspiratory muscle training could increase maximal inspiratory pressure but did not tend to improve respiratory functions, functional exercise capacity and quality of life in patients with pulmonary hypertension.<sup>9</sup> Our current study disagrees with these findings.

Stephan Keusch and co-workers conducted a study to determine the effects on rehabilitation in patients with pulmonary arterial hypertension. Although their study showed that the underlying mechanisms were not completely clarified, positive effects might be measured in different organ systems such as the cardiopulmonary system, immune system, skeletal muscles and also on a psychological level. Their results also showed improvements in the 6-minute walking test, muscle strength, peak oxygen uptake and muscle endurance, as well as physical and mental quality of life scores. They also employed the SF-36 questionnaire.<sup>23</sup> The current study coincides with their findings. They also concluded that a core issue of multidisciplinary rehabilitation is close cooperation between the experienced rehabilitation clinic offering a specialized program for pulmonary hypertension and the pulmonary hypertension expert centre, which takes care of the patient and is observed to be thoroughly involved in the training program. Our current study and their study both recommend further multicenter international randomized trials to evaluate whether these specialized programs are feasible within different healthcare systems and to assess long-

term effects and survival. Ekkehard Grunig conducted a study on determining the effects of exercise and respiratory training on clinical progression and survival in patients with severe chronic pulmonary hypertension. Their study concluded that exercise and respiratory training is an add-on to medical treatment and they tend to bring improvement in exercise capacity and quality of life of the patients with pulmonary hypertension.<sup>24</sup> Our current study agrees with their conclusion. The limitation of this study was assessment was a challenge because assessing patients is itself a tough task, patients were reluctant and needed more counselling regarding this study. Pulmonary Hypertension itself carries a high risk of emergencies so the assessor had to be more alert all the time. Our study would have been more vast and versatile if it had more funding so that the study outcomes could be expanded because funding would have added more to the logistics, medical testing and investigation.

Our current study recommends that there must be more formulated practice guidelines for patients with pulmonary hypertension regarding pulmonary rehabilitation programs. This research study also recommends that the benefits of pulmonary rehabilitation should be shared with pulmonologists to engage the patients in pulmonary rehabilitation plans as soon as possible. Future researchers are advised to conduct more case studies and randomized controlled with a larger sample size for generalizable results and more authentic evidence to be added to the literature.

## CONCLUSION

The study concludes that a pulmonary rehabilitation plan significantly improves endurance, emotional well-being, general health, activity status and quality of life among patients with pulmonary hypertension.

## DECLARATIONS

**Consent to participate:** Written consent had been taken from patients. All methods were performed following the relevant guidelines and regulations.

**Availability of data and materials:** Data will be available on request. The corresponding author will submit all dataset files.

**Competing interests:** None

**Funding:** No funding source is involved.

**Authors' contributions:** All authors read and approved the final manuscript. **CONSORT**

**Guidelines:** All methods were performed following the relevant guidelines and regulations.

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