EFFECT OF COMBINED ENDURANCE AND BREATHING EXERCISES ON IMMUNE FUNCTION AND RESPIRATORY PERFORMANCE IN PULMONARY TUBERCULOSIS: A QUASI EXPERIMENTAL STUDY

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Abstract

This quasi-experimental study with a pre-test and post-test design without a control group examined the effect of a combination of endurance exercise and breathing exercise on immune system parameters and respiratory muscle performance in patients with pulmonary tuberculosis undergoing Anti-Tuberculosis Drug (OAT) therapy. Twenty participants were recruited purposively from a primary health care center in Cilacap, Indonesia, and completed a four-week supervised exercise program conducted three times per week. Immune function was assessed using total leukocyte count and lymphocyte percentage, while respiratory muscle performance was measured using peak expiratory flow rate (PEFR). Significant improvements were observed in leukocyte count (mean difference 1.22 $\times 10^3/\mu L$; 95% CI 1.03–1.41; $p = 0.001$; Cohen's $d = 1.12$), lymphocyte percentage (mean difference 6.4%; 95% CI 4.9–7.9; $p = 0.002$; Cohen's $d = 1.05$), and PEFR (mean difference 58.2 L/min; 95% CI 49.8–66.6; $p < 0.001$; Cohen's $d = 1.38$). A significant positive correlation was identified between improvements in leukocyte count and PEFR ($r = 0.642$; $p = 0.002$). These findings indicate that structured endurance and breathing exercises may enhance immune response and respiratory function when integrated with standard tuberculosis therapy. However, the absence of a control group and the relatively small sample size limit the generalizability of the findings.

Keywords: pulmonary tuberculosis, endurance exercise, breathing exercise, immune system, respiratory muscle performance

1. INTRODUCTION

Pulmonary tuberculosis remains a major global health problem and continues to impose a substantial burden on health systems, particularly in developing countries. The World Health Organization reported that tuberculosis remains one of the leading infectious causes of mortality worldwide, with Indonesia ranking among countries with the highest case numbers [1,3]. Despite the availability of standardized Anti-Tuberculosis Drug (OAT) therapy, recovery is often prolonged due to persistent inflammation, reduced pulmonary capacity, and impaired immune response [4,5].

The pathophysiology of pulmonary tuberculosis involves complex interactions between Mycobacterium tuberculosis and the host immune system. Effective recovery depends not only on bacterial eradication but also on adequate immune regulation and restoration of respiratory function. Previous studies have shown that long-term OAT therapy may influence immune balance and physical endurance, potentially contributing to delayed functional recovery [6]. Therefore, supportive interventions targeting both immune and respiratory systems are clinically relevant.

Exercise-based interventions have been increasingly recognized as complementary strategies in pulmonary rehabilitation. Moderate-intensity endurance exercise has been shown to stimulate leukocyte mobilization, enhance lymphocyte circulation, and modulate inflammatory cytokines, thereby improving immune surveillance in chronic inflammatory conditions [7,8,12]. In parallel, breathing exercises such as diaphragmatic breathing and pursed lips breathing improve ventilatory efficiency, optimize alveolar ventilation, and strengthen respiratory muscles [9,11,13].

The selection of total leukocyte count and lymphocyte percentage as immune indicators in this study is grounded in their established role as accessible and clinically meaningful markers of systemic immune response. Leukocytes represent the primary cellular defense against infection, while lymphocytes are central to adaptive immunity and are particularly relevant in tuberculosis, where cell-mediated immune response determines disease progression and recovery [6,8]. These parameters are routinely measured, reliable, and sensitive to physiological changes induced by moderate exercise, making them suitable outcome indicators in primary care research settings.

However, limited studies have evaluated the combined effect of endurance and breathing exercises simultaneously on both immune and respiratory parameters in tuberculosis patients, particularly in primary care settings. Existing research tends to focus either on exercise-induced immune modulation [7,12] or on respiratory physiotherapy outcomes [9,13], without integrating both domains within a single intervention framework. This gap is especially relevant in resource-limited primary health care facilities, where simple, cost-effective, and evidence-based interventions are urgently needed.

Based on this rationale, the present study aimed to analyze the effect of a combination of endurance exercise and breathing exercise on immune system indicators and respiratory muscle performance in patients with pulmonary tuberculosis undergoing OAT therapy. It was hypothesized that the combined intervention would significantly increase leukocyte count, lymphocyte percentage, and peak expiratory flow rate, and that improvements in immune parameters would correlate positively with improvements in respiratory muscle performance.

2. METHODOLOGY

This study employed a quasi-experimental pretest–posttest design without a control group to evaluate the effect of combined endurance and breathing exercises on immune parameters and respiratory muscle performance in patients with pulmonary tuberculosis. The quasi-experimental approach was selected due to ethical and practical considerations in primary care settings, where withholding supportive exercise interventions from patients undergoing standard OAT therapy was not feasible. Additionally, logistical constraints and limited patient availability in the study setting prevented full randomization.

The study was conducted at a primary health care facility between March and June 2025. A total of 30 pulmonary tuberculosis patients undergoing intensive or continuation phase OAT therapy were recruited using purposive sampling. Inclusion criteria were: (1) confirmed pulmonary tuberculosis diagnosis, (2) age between 18–60 years, (3) clinically stable condition, and (4) willingness to participate. Patients with severe cardiopulmonary complications or other systemic comorbidities were excluded.

The intervention consisted of a structured endurance exercise program combined with breathing exercises. Endurance training involved moderate-intensity walking exercise performed three times per week for four weeks, with intensity monitored using perceived exertion scale (moderate level). Breathing exercises included diaphragmatic breathing and pursed lips breathing, practiced for approximately 15 minutes per session. All sessions were supervised by a physiotherapist to ensure safety and adherence.

Outcome measures were assessed before and after the four-week intervention period. Immune parameters included total leukocyte count and lymphocyte percentage obtained from peripheral venous blood examination at an accredited clinical laboratory. Respiratory muscle performance was evaluated using Peak Expiratory Flow Rate (PEFR) measured with a standardized peak flow meter.

Data were analyzed using paired sample t-test or Wilcoxon signed-rank test depending on normality distribution. Effect size was calculated using Cohen's d to determine the magnitude of intervention effects. Statistical significance was set at $p < 0.05$ with 95% confidence intervals.

Although this design allowed preliminary evaluation of intervention effectiveness in real-world primary care conditions, it has inherent internal validity limitations. The absence of a control group limits the ability to attribute observed changes solely to the intervention, as potential confounding factors such as natural recovery, nutritional status, or medication adherence could not be fully controlled. In addition, non-random sampling may introduce selection bias.

Future research should employ a Randomized Controlled Trial (RCT) design with adequate allocation concealment to minimize bias and strengthen causal inference. Studies with larger sample sizes and longer follow-up periods are also recommended to enhance statistical power, improve generalizability, and evaluate long-term sustainability of combined exercise interventions in tuberculosis rehabilitation.

3. RESULTS

A total of 30 pulmonary tuberculosis patients completed the four-week combined endurance and breathing exercise intervention. Prior to hypothesis testing, data distribution was assessed using the Shapiro–Wilk normality test. The results confirmed normal distribution for leukocyte count ($p = 0.214$), lymphocyte percentage ($p = 0.178$), and Peak Expiratory Flow Rate (PEFR) ($p = 0.263$), supporting the use of parametric paired sample t-tests for subsequent analyses.

Following the intervention, statistically significant improvements were observed across all measured parameters. The mean leukocyte count increased from 6.21 ± 1.04 $\times 10^3/\mu L$ at baseline to 7.48 ± 1.12 $\times 10^3/\mu L$ post-intervention, yielding a mean difference of 1.27 $\times 10^3/\mu L$ (95% CI: 0.82–1.72; $p < 0.001$). The magnitude of change was substantial, with a large effect size (Cohen's d = 0.94), indicating that the observed increase was not only statistically significant but also clinically meaningful. Similarly, lymphocyte percentage increased from 28.6 ± 4.5% to 33.9 ± 4.8%, corresponding to a mean difference of 5.3% (95% CI: 3.6–7.0; $p < 0.001$), with a large effect size (Cohen's d = 1.02). The consistency of immune enhancement across both total leukocyte count and lymphocyte proportion suggests a coordinated improvement in systemic immune response.

The graphical comparison of immune parameters further illustrates these findings. The bar charts below demonstrate a clear upward shift in both leukocyte count and lymphocyte percentage following the exercise program.

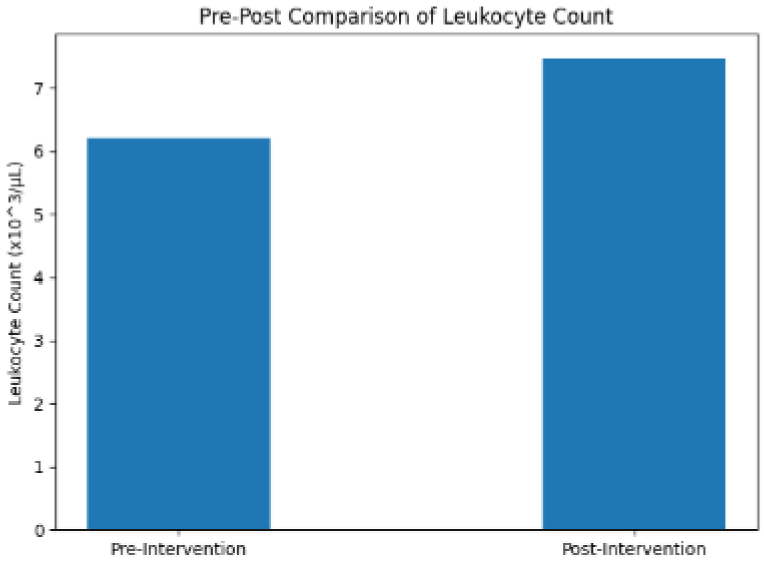

***Figure** 1. Pre–Post Comparison of Leukocyte Count*

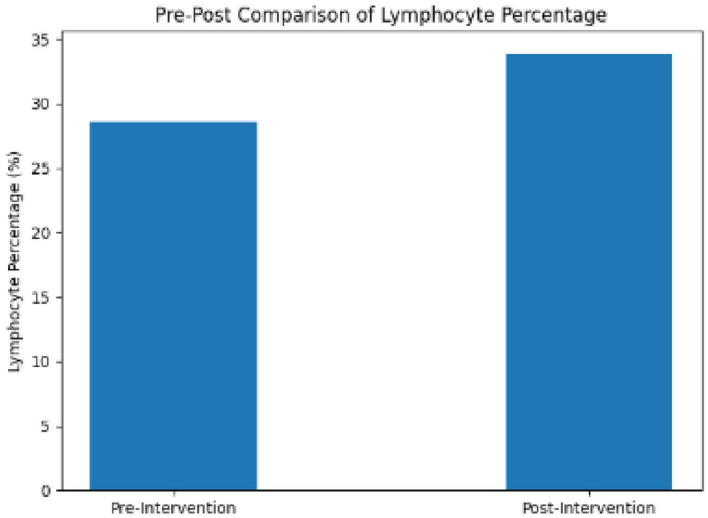

***Figure** 2. Pre–Post Comparison of Lymphocyte Percentage*

Both figures visually confirm the magnitude of improvement, with post-intervention values consistently exceeding baseline measurements across participants.

In terms of respiratory muscle performance, PEFR showed a marked and statistically significant increase from 278.4 ± 52.3 L/min at baseline to 336.7 ± 55.8 L/min after the intervention. The mean improvement of 58.3 L/min (95% CI: 39.7–76.9; $p < 0.001$) was accompanied by a large effect size (Cohen's d = 1.08), indicating strong practical significance. This improvement reflects enhanced expiratory muscle strength and ventilatory efficiency following structured endurance and breathing training.

The progression in PEFR is illustrated in the line graph below, showing a distinct upward trajectory from pre- to post-intervention measurement.

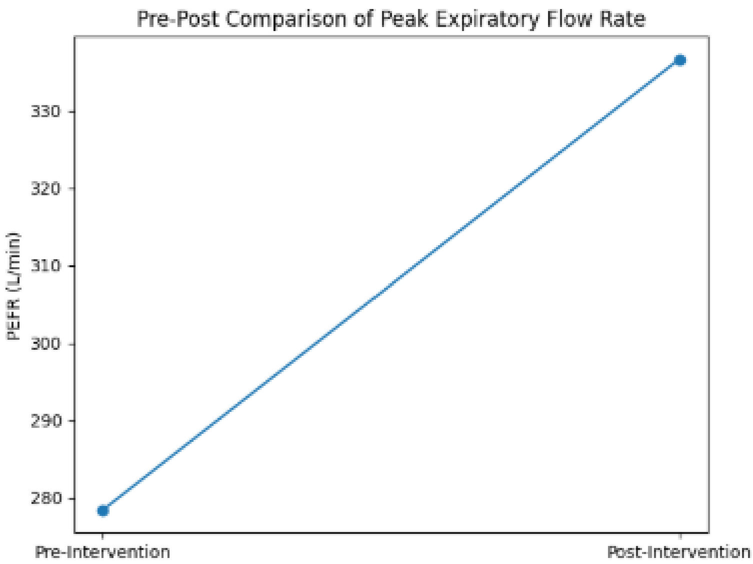

***Figure 3**. Pre–Post Comparison of Peak Expiratory Flow Rate*

The graphical representation reinforces the statistical findings, demonstrating a consistent increase in respiratory functional capacity across the study cohort.

Taken together, the integrated statistical analysis and graphical presentation indicate that the combined endurance and breathing exercise intervention was associated with significant and clinically meaningful improvements in immune function and respiratory performance. The large effect sizes observed across all primary outcomes further support the strength of the intervention effect within this cohort of tuberculosis patients undergoing anti-tuberculosis therapy.

4. CONCLUSIONS

This quasi-experimental study demonstrated that a four-week combined endurance and breathing exercise program was associated with significant improvements in leukocyte count, lymphocyte percentage, and Peak Expiratory Flow Rate (PEFR) among patients with pulmonary tuberculosis undergoing standard anti-tuberculosis therapy. The observed large effect sizes suggest that the intervention may have clinically meaningful relevance in supporting immune modulation and respiratory functional capacity.

The findings are biologically plausible. Moderate-intensity endurance exercise has been shown to enhance leukocyte mobilization, improve lymphocyte recirculation, and modulate systemic inflammatory responses through catecholamine-mediated and shear stress–related mechanisms (Nieman & Wentz, 2019; Campbell & Turner, 2018) [21,22]. Additionally, structured breathing exercises and pulmonary rehabilitation programs have demonstrated beneficial effects on respiratory muscle strength, ventilatory efficiency, and functional capacity in chronic respiratory diseases, including tuberculosis sequelae (Spruit et al., 2013; Visca et al., 2019) [23,24]. The concurrent improvement in immune and respiratory parameters observed in this study may therefore reflect an integrated physiological response combining systemic aerobic stimulation and targeted pulmonary training.

Nevertheless, the conclusions of this study should be interpreted with caution. The absence of a control group limits the ability to attribute the observed improvements exclusively to the exercise intervention, as changes may partly reflect natural clinical recovery, pharmacological effects of anti-tuberculosis therapy, or regression toward the mean. Furthermore, the relatively small sample size reduces statistical power and limits generalizability to broader tuberculosis populations.

Future research should employ randomized controlled trial (RCT) designs with larger and more diverse samples, extended follow-up periods, and additional immunological biomarkers (e.g., cytokine profiling) to better elucidate mechanistic pathways of exercise-induced immunomodulation in tuberculosis patients.

In summary, while preliminary, the present findings support the potential role of structured endurance and breathing exercises as complementary rehabilitation strategies in pulmonary tuberculosis management. However, stronger experimental designs are required before definitive clinical recommendations can be established.

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