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A randomized comparative study of active cycle of breathing technique versus oscillating positive expiratory pressure therapy on lung function and quality of life in children with primary ciliary dyskinesia

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M.Sc. Thesis

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Thesis Approval

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Dedication

With deep gratitude and love, I dedicate this thesis to my family, as they have been my inspiration and source of support and encouragement every moment.

To my father, an expert and a highly skilled physiotherapist. Hanna Fashho is not only my father but also my colleague and mentor. It has been an honor to walk in your footsteps, and it has also been a journey filled with success and knowledge.

To my mother, your support, encouragement, and wisdom have been a guiding light in the chapters of my life.

This work is dedicated to my wife, my greatest supporter and the love of my life. Your belief in my abilities has been a source of strength, your encouragement has been my motivation to success.

I dedicate this thesis to you, Hanna, my little son, with love, gratitude, and the hope that the world will always respond to you with the same joy that you have brought into my life.

This thesis is dedicated to my supervisor, Dr. Hadeel Halaweh, whose knowledge, guidance, and constant encouragement were crucial to the successful completion of this study.

Declaration

This thesis is submitted in partial fulfillment of the requirement for the Master's degree in physical therapy.

I declare that the content of this thesis (or any part of the same) has not been submitted for a higher degree to any other University or institution.

Signed *Bishara Fashho*

Date: 27 /12 /2023

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A randomized comparative study of active cycle of breathing technique versus oscillating positive expiratory pressure therapy on lung function and quality of life in children with primary ciliary dyskinesia

Prepared by: Bishara Hanna Fashho

Supervisor: Dr. Hadeel Halaweh

Abstract:

Background: Primary Ciliary Dyskinesia (PCD) is a rare inherited disease that causes recurrent respiratory tract infections and sputum retention due to inadequate mucociliary clearance. Airway clearance techniques are commonly recommended for patients with PCD to facilitate mucus clearance as a part of the treatment protocol.

Study objectives: Our primary goal of this study was to compare the efficiency of the active cycle of breathing technique (ACBT) and oscillating positive expiratory pressure therapy (OPEP) on lung function and functional capacity in children with PCD. Our secondary goal was to evaluate the quality of life and activities of daily living. There is a limitation in the use of standardized chest physiotherapy guidelines with PCD patients. In Palestine, there is a lack of awareness of using positive expiratory pressure devices, which could be beneficial to PCD patients.

Methods: An experimental randomized comparative study design was conducted. A total of 32 PCD children, ages ranging from 6 to 18 years were enrolled in the two groups. The first group was assigned to the ACBT, while the second group was assigned to the OPEP. Study tools and outcome measures included a data collection sheet, spirometry measurements, a six-minute walk test (6MWT), and the PCD quality of life questionnaire (PCD QOL). The study took a period of three months, a pretest was conducted at baseline, a mid-test after six weeks, and a post-test after 12 weeks. Descriptive statistical analysis, T-tests, ANOVA, and correlation tests were performed as needed. The effect size was computed as Cohen's d. The statistical significance level was set at p-value < 0.05.

Results: The FEV_1 and $MEF_{25-75\%}$, as well as the 6MWT, showed statistical significance between the two groups (p=0.02, p=0.04, and p=0.05) in favor of the OPEP group with the effect size of Cohen's d equals (0.86, 0.76, and 0.71) respectively. However, the FVC and FEV_1/ FVC showed no statistical significance $p > 0.05$. In addition, positive correlations were found between the FEV_1, FVC, and 6MWT, and also between 6MWT and the PCD QOL.

Conclusion: For PCD patients, daily airway clearance techniques are crucial. The ACBT and OPEP are two efficient home-based physiotherapy techniques. In the FEV_1, $MEF_{25-75\%}$, and 6MWT, the OPEP device seems to be more efficient. OPEP might be an efficient alternative method for airway clearance in PCD patients. Additional research is needed to further examine the effectiveness of the two techniques.

Keywords: Primary ciliary dyskinesia, airway clearance techniques, active cycle of breathing, chest physiotherapy, oscillating positive expiratory pressure.

دراسة مقارنة عشوائية بين تقنية الدورة النشطة للتنفس والعلاج بواسطة ضغط الزفير الإيجابي المتذبذب على وظائف الرئة وجودة الحياة عند الأطفال الذين يعانون خلل حركة الأهداب الأولية.

الإعداد: بشارة حنا فشحو

اشراف: د. هديل حلاوة

ملخص عن الدراسة باللغة العربية

المقدمة: خلل حركة الأهداب الأولية (PCD) هو مرض وراثي نادر يسبب في التهابات متكررة في الجهاز التنفسي نتيجة لتراكم المخاط في الجهاز التنفسي وهذا يعود إلى خلل في الأهداب أو الشعيرات. يوصى عادةً بتقنيات علاج طبيعي للإبقاء مجرى الهواء للمرضى الذين يعانون من خلل حركة الأهداب الأولية نظيفا ولتسهيل إزالة المخاط كجزء من العلاج.

الأهداف: كان هدفنا الأساسي من هذه الدراسة هو مقارنة فعالية تقنية تنفس الدورة النشطة والعلاج بواسطة الضغط الزفيري الإيجابي المتذبذب على وظائف الرئة والقدرة الوظيفية لدى الأطفال المصابين بخلل حركة الأهداب الأولية. كان هدفنا الثانوي هو تقييم نوعية الحياة وأنشطة الحياة اليومية. هناك قيود في استخدام المبادئ الموحدة للعلاج الطبيعي للصدر مع مرضى خلل حركة الأهداب الأولية. في فلسطين، هناك نقص في الوعي حول استخدام أجهزة ضغط الزفير الإيجابية، والتي يمكن أن تكون مفيدة لمرضى خلل حركة الأهداب الأولية.

المنهج المتبع للدراسة: تم اختيار تصميم الدراسة كدراسة مقارنة عشوائية. تم تسجيل ما مجموعه 32 مشاركًا من مرضى خلل حركة الأهداب الأولية، تتراوح أعمارهم بين 6 إلى 18 عامًا في المجموعتين. تم تعيين المجموعة الأولى لتقنية تنفس الدورة النشطة، بينما تم تعيين المجموعة الثانية للعلاج بواسطة الضغط الزفيري الإيجابي المتذبذب. تضمنت أدوات الدراسة ومقاييس النتائج ملف جمع البيانات، وقياسات فحص وظائف الرئتين، واختبار المشي لمدة ست دقائق، واستبيان جودة الحياة. استغرقت الدراسة فترة ثلاثة أشهر، وتم إجراء الاختبار القبلي قبل البدء بتطبيق الدراسة والاختبار المتوسط بعد ستة أسابيع والاختبار البعدي بعد 12 أسبوعًا. تم إجراء التحليل الإحصائي الوصفي، واختبارات المقارنة بين المجموعتين واختبارات الارتباط حسب الحاجة. تم تحديد مستوى الدلالة الإحصائية عند قيمة $p <0.05$.

نتائج الدراسة: هناك فروق ذات دلالة إحصائية بين المجموعتين عند مستوى دلالة ($p <0.05$) في قراءات FEV_1 و$MEF_{25-75\%}$، بالإضافة إلى اختبار المشي لمدة ست دقائق، يعزى لصالح مجموعة الضغط الزفيري الإيجابي المتذبذب. قيمة معامل حجم الأثر بالاعتماد على معادلة كوهين (0.86، 0.076، و0.71) بالترتيب. ومع ذلك، لم يكن هناك فروق ذات دلالة احصائية عند مستوى دلالة ($p >0.05$) في قراءات FVC وFEV_1/FVC. بالإضافة، تم العثور على ارتباطات إيجابية بين FEV_1 وFVC وكذلك بين اختبار المشي لمدة ست دقائق واستبيان جودة الحياة لمرضى خلل حركة الأهداب الأولية.

الاستنتاج: تقنيات العلاج الطبيعي اليومي للرئتين لمرضى خلل حركة الأهداب الأولية أمرًا بالغ الأهمية. تعد تقنية الدورة النشطة للتنفس والعلاج بواسطة ضغط الزفير الإيجابي المتذبذب من تقنيات العلاج الطبيعي المنزلية الفعالة. اظهرت نتائج البحث أن جهاز الضغط الزفير الإيجابي المتذبذب أكثر كفاءة من تقنية الدورة النشطة في قراءات FEV_1 و$MEF_{25-75\%}$ واختبار المشي لمدة ست دقائق .قد يكون جهاز الضغط الزفير الإيجابي المتذبذب طريقة علاجية اضافية فعالة لدى مرضى خلل حركة الأهداب الأولية. هناك حاجة إلى مزيد من البحث لمواصلة دراسة فعالية الطريقتين.

الكلمات المفتاحية: مرض خلل حركة الأهداب الأولية، العلاج الطبيعي للأمراض الجهاز التنفسي، تقنية الدورة النشطة للتنفس، ضغط الزفير الإيجابي المتذبذب.

Table of Contents

List of Figures:

List of Tables:

List of appendixes:

List of abbreviations

PCD: Primary ciliary dyskinesia

CF: Cystic fibrosis

ACBT: Active cycle of breathing technique

PEP: Positive expiratory pressure

OPEP: Oscillatory positive expiratory pressure

ACT: Airway clearance techniques

PFT: Pulmonary function test

FEV_1: Forced expiratory volume in 1 second

FVC: Forced vital capacity

$MEF_{25-75\%}$: Maximum expiratory flow between 25% and 75% of FVC

FET: Forced expiration technique

6 MWT: 6- minute walk test

QOL: Quality of life

BMI: Body mass index

AD: Autogenic drainage

1. Chapter one

1.1 Introduction

1.2 Problem statement

1.3 Study justification

1.4 Study hypothesis

1.5 Objectives

1.6 Research question

1.7 Terminology

1.1 Introduction

Primary ciliary dyskinesia (PCD) is an autosomal recessive condition, it is a genetic disease associated with abnormalities in the function and structure of cilia that can affect ~1 in 10,000 births (Kumar & Walker, 2020). The influence of parental characteristics such as consanguinity leads to and contributes to an increase in the rate of autosomal recessive genetic disorders (El Goundali et al., 2022). This condition can significantly affect lung function, functional exercise capacity and quality of life of the affected children (Ring et al., 2018). In Palestine, where the population is highly consanguineous, 68 people have been diagnosed with PCD, confirmed by either transmission electron microscopy and/or positive genetic testing (Rumman et al., 2023).

Cilia have the role of mucociliary clearance and transport of fluid (Leigh et al., 2019). The clinical features are characterized by chronic nasal congestion, chronic otitis media, recurrent chest infections, productive cough, bronchiectasis, dextrocardia, and situs inversus (in about 50% of patients), and male infertility (Lucas et al., 2014). Repeated chest infections lead to lung inflammation and eventually to a deterioration in lung function.

All treatment suggestions are based on limited evidence or extrapolated from the CF guidelines. Treatment may include antibiotics, anti-inflammatory drugs, immunization and inhaled medications. Mucolytics like hypertonic saline may theoretically be effective in increasing mucus clearance. Occasionally, surgical procedures like lobectomy may be a treatment option of localized lung damage (Barbato et al., 2009).

Airway clearance techniques (ACT) have a crucial role in clearing the mucus out of the lungs (O'Neill et al., 2019). There are various airway clearance techniques, including active cycle of breathing, autogenic drainage, chest vibration, and percussion, airway oscillating devices, positive expiratory pressure therapy, exercise, and other techniques (Damseh et al., 2017). These techniques are important to keep upper and lower airway tracts clean from mucous and secretions. The goal of ACT therapy, as with all chronic respiratory diseases, is to restore or maintain normal lung function as much as possible, which will reflect on the daily activities and quality of life (QOL). Selecting the most appropriate technique is influenced by age, performance, cooperation, and cost.

The active cycle of breathing technique (ACBT) is an active airway clearance technique that can be used to mobilize, clear excess pulmonary secretions, and generally improve lung function. This technique consists of three main phases: breathing control, thoracic expansion exercise, and forced expiratory technique (Lewis et al., 2012). This technique has the advantage of being able to be performed at home with the supervision of parents if needed. The technique is safe and effective, and it does not require the use of any special equipment (Burelli, 2016).

An oscillating positive expiratory pressure (OPEP) device such as the Aerobika ® which is handheld, drug-free, and simple to use (Coppolo et al., 2022). The device facilitates sputum clearance from the lungs, reduces air trapping, and enhances lung ventilation. This occurs as a result of the combination of positive expiratory pressure and high-frequency oscillations that are generated during a slightly active expiration through a device. This device is described in a recent systematic review as safe to use, without adverse effects (Rocamora-Pérez et al., 2022).

1.2 Problem statement

PCD is a chronic disease that requires lifelong medical care. It limits daily activities and affects the quality of life. To keep lung tissue healthy for as long as possible, early airway clearance therapy is needed. Effective chest physiotherapy techniques should be used to reduce symptoms, prevent progression, and improve quality of life. Variant methods can be used to maintain airway clearance as the active cycle of breathing technique and oscillating positive expiratory pressure in patients with primary ciliary dyskinesia. Yet, the effectiveness of these methods and its relatedness to QoL of the affected children is not studied in Palestine.

We compared the efficacy of the active cycle of breathing technique to oscillating positive expiratory pressure in patients with primary ciliary dyskinesia, age range six to eighteen years old. There isn't enough evidence concerning these types of ACT in PCD, but there are several studies in cystic fibrosis that have similar characteristics that could be portable and applied to PCD (Maglione et al., 2017; L. M. Schofield et al., 2018). In addition, there is a limitation in using standardized guidelines in chest physiotherapy treatment sessions with PCD patients.

Evidence suggests that the OPEP device improves pulmonary function, and lung oxygenation, clears mucus from the bronchi, reduces respiratory complications, and aids patient compliance with treatment. Furthermore, this device is drug-free, portable, and simple to use, and it reduces therapy costs (Hristara-Papadopoulou et al., 2008). In Palestine, there is a lack of knowledge in using the OPEP devices.

1.3 Study justification

Due to the existence of various airway clearance techniques, it is important to select an effective one for PCD patients. This study aimed to compare the effectiveness of these two techniques, point out gaps in knowledge in this area, and assess the potential for changes in lung function, as well as the functional exercise capacity. In addition, to analyze the effects of the intervention on the activities of daily living, physical, school, and social functioning.

In Palestine, still there is limited evidence on PCD, this study is expected to contribute to enriching the PCD literature in Palestine.

1.4 Research hypothesis

- The OPEP device is as effective as the active cycle of breathing technique on the lung function (Spirometer) among PCD patients (6-18 years).
- The OPEP device is as effective as the active cycle of breathing technique on the functional exercise capacity (Six-minute walk test) among PCD patients.
- Both techniques will have a positive impact on the quality of life and daily living of PCD patients in terms of physical, social, and school functioning.

1.5 Study Aim:

To compare the effectiveness of oscillating positive expiratory pressure therapy with the active cycle of breathing technique in enhancing lung function, functional exercise capacity, quality of life, and activities of daily living among pediatric patients diagnosed with primary ciliary dyskinesia.

1.6 Objectives

- To assess the demographic and clinical characteristics of the children diagnosed with PCD.
- To evaluate lung function, functional exercise capacity and quality of life among children with PCD.
- To compare the effectiveness of the OPEP device and the active cycle of breathing technique on lung function (Spirometer) among PCD pediatric patients aged 6-18 years.
- To compare the effectiveness of the OPEP device and the active cycle of breathing technique on the functional exercise capacity of pediatric PCD patients, measured through the Six-minute walk test.
- To Investigate the impact of both the OPEP device and the active cycle of breathing technique on the quality of life and daily living of pediatric PCD patients, focusing on physical, social, and school functioning.

1.7 Research question

Is oscillating positive expiratory pressure therapy more effective than using the active cycle of breathing technique on lung function, functional exercise capacity, quality of life and activities of daily living among patients with primary ciliary dyskinesia (6-18 years)?

1.8 Terminology

- **Motile cilia:** are thin, hair-like organelles that project from cells and extend up to 20 mm from the surface of the cell. There are approximately 200 motile cilia in each ciliated cell. The respiratory epithelium, brain ependyma, fallopian tubes, and flagellum of male spermatozoa all have cells with motile cilia (Mirra et al., 2017). In normal airways, motile cilia beat in a coordinated, whip-like manner at frequencies between 10 and 20 Hz to promote the flow and clearance of fluids among the cell surfaces (Bustamante-Marin & Ostrowski, 2017). Dysfunction of motile cilia results in the rare disease of primary ciliary dyskinesia (PCD) (Lee & Ostrowski, 2021).

- **Airway clearing techniques:** a range of breathing patterns and strategies, both with or without the use of a device, that are aimed to help with sputum clearance, improve gas exchange, and prevent respiratory tract infections (Belli et al., 2021).
- **Bronchiectasis:** is a chronic respiratory condition characterized by irreversible bronchial dilation, in which the elastic and muscular tissue is damaged. Cough, sputum production, and recurrent respiratory infections are among the symptoms associated with it (Contarini et al., 2018).
- **Situs inversus totalis:** is a condition in which the organs of the chest and abdomen are reversed in a mirror image pattern. E.g. left-right mirror reversal of the visceral organs (Postema et al., 2020).
- **Collateral ventilation:** is defined as "the ventilation of alveoli via pathways that bypass normal airways" (Terry & Traystman, 2016). When peripheral airways are obstructed, collateral channels of ventilation provide an alternative route for air flow. A variety of ACTs are aimed to recruit these channels allowing air to move behind sputum blockages. The idea underlying any of these therapy methods is that by increasing lung volume, airflow through the collateral pathways will increase. This airflow is supposed to push the sputum plugs more proximally (Main, 2016).
- **Lung function:** the ability of the lungs to move air in and out and exchange oxygen and carbon dioxide with the blood. Spirometer is a common test used to measure lung function (Graham, Steenbruggen, Barjaktarevic, et al., 2019).
- **Functional exercise capacity:** the ability of a person to carry out physical activities and tasks in daily life without experiencing undue fatigue. One commonly used measure of functional exercise capacity is the six-minute walk test (6MWT) (Matos Casano & Anjum, 2023).
- **Quality of life:** is a multidimensional concept that encompasses various aspects of an individual's well-being and satisfaction with different life domains. It includes physical health, mental and emotional well-being, social relationships, economic status, and more (Teoli & Bhardwaj, 2023).

2. Chapter two: Literature review

2.1 Theoretical studies

2.2 Similar studies

2.1 Theoretical studies

2.1.1 Introduction

Patients with primary ciliary dyskinesia frequently require a variety of therapies as well as the involvement of a multidisciplinary team. A respiratory physician, an ENT physician, a physiotherapist, a nurse, and an audiologist with a special interest in PCD will assess and manage the patients. Patients are treated on an individual basis. Since there is no cure for PCD, management focuses on optimizing health, social, and psychological well-being while preventing lung damage progression. Lung function testing, microbiological studies, and a regime of airway-clearing techniques should all be part of routine care (Lucas et al., 2017).

2.1.2 Medical management in PCD

- Upper airways management

The nasal cavity, paranasal sinuses, and middle ear are all impacted by mucous due to impaired mucociliary clearance in the upper airways. Nasal blockage, loss of smell, discomfort, coughing, and nasal discharge are some of the symptoms. Sinonasal irrigation with saline, topical nasal steroids, and antibiotics are all used in the treatment of this condition (Werner et al., 2015). Furthermore, PCD patients frequently suffer from glue ear, which causes conductive hearing loss. Audiology visits are important to evaluate hearing and, if necessary, offer hearing aids (Harris, 2017).

- Lower airways management

Antibiotic therapy for respiratory tract infections should be started as soon as possible and adjusted based on microbiological findings. In most cases of PCD, surgery is not suggested; however, in some situations of localized disease that has not responded to conservative treatment, lobectomy may be considered. End-stage lung failure can be managed with bilateral lung transplantation (Werner et al., 2015).

- Non-respiratory manifestations

Patients with congenital heart disease should be referred to a cardiologist. Infertility in both men and women can be treated with the appropriate reproductive techniques (Lucas et al., 2017).

2.1.3 Physiotherapy management in PCD

Physiotherapy management is an important part of the treatment of respiratory illnesses, and it has been found to help with the clearance of excess airway secretions, the sensation of breathlessness, and decreased exercise activity and tolerance.

Physiotherapy ACTs used in the treatment of pediatric patients may consist of several different modalities:

- The use of modified postural drainage, chest wall percussion, vibrations, and high-frequency chest wall compression (HFCC).
- Other breathing techniques, such as the active cycle of breathing technique (ACBT) and autogenic drainage (AD).
- Devices that introduce positive pressure and/or oscillation into the airways: Positive expiratory pressure (PEP) masks, Flutter, Cornet, Aerobika, Acapella, and intrapulmonary percussive ventilation (IPV).
- Physical activity, sports, and systemic exercise programs are recommended (Rogers & Doull, 2005).

The mainstay of treatment is daily airway clearance, which can be done in a variety of ways and is adapted as the child grows, and personalized to fit the individual patient's care. In clinical practice, more than one ACT may be effective for a patient at the same time, and the technique chosen may be based on availability and patient preference (McIlwaine et al., 2017).

2.1.3.1 Active cycle of breathing (ACBT)

ACBT is a cycle of breathing control, thoracic expansion, and forced expiration technique.

- Breathing control is used to relax the airways and prevent bronchospasm, and oxygen desaturation. Using a diaphragmatic breathing pattern while relaxing the upper chest and shoulders, the patient is instructed to breathe in through the nose and breathe out through the mouth with little effort by using the pursed-lip technique (Thorat et al., 2019). Placing the patient's hand over the diaphragm will encourage lower breathing and upper chest relaxation. Before moving to thoracic exercise, the patient may be instructed to usually take six breaths.

- Thoracic expansion exercises are deep breathing exercises that focus on inspiration. The patient is instructed to take a slow, deep breath in with minimal accessory muscle use. After achieving maximal inspiration, the patient may hold breath for three-second to get more air into the smaller airways and behind the mucus, before performing passive expiration. The patient's hands are placed on the chest wall to facilitate movement and provide proprioceptive feedback. These deep breathing exercises are repeated up to five times.
- Forced expiration technique (FET), also called huff cough. Huffing assists in moving sputum from small airways to larger airways, where it is eliminated by coughing since coughing alone cannot remove sputum from small airways (Lewis et al., 2012). This huffing should be continued until the lungs are clear of any mucus.

2.1.3.2 Oscillating Positive expiratory pressure (OPEP)

OPEP is a portable device used as an airway clearance therapy technique. It was first developed and described in Switzerland as an addition and supplement to conventional airway clearance techniques (Gupta et al., 2022). The device's main physiological effects are generating positive expiratory pressure (PEP) and air-flow oscillations.

During OPEP therapy, the patient exhales against a fixed resistance which generates pressures ranging from 10 to 20 cm H2O. This type of therapy involves a slightly elevated tidal volume inspiration and a slightly active expiration against resistance (Demchuk & Chatburn, 2021; West et al., 2010).

Theoretically, PEP in OPEP therapy works by creating positive pressure in the airways by breathing out against resistance. This positive pressure may help to increase functional residual capacity allowing collateral ventilation to occur. Collateral ventilation allows air to flow behind secretions that obstruct the airways, allowing secretions to be moved to the larger airways more easily. The volume of trapped air in peripheral airways is thought to be reduced as a result of this process (Olsén et al., 2015). Furthermore, airflow oscillations induce vibrations and turbulent airflow spikes that facilitate mucociliary clearance by displacing secretions into the airway lumen and reducing the viscosity of secretions (Poncin et al., 2020).

2.1.3.3 Quality of life in patients with PCD

PCD is associated with a high rate of morbidity and impaired quality of life (Madsen et al., 2013a). It has been found to have a significant impact on physical, emotional, social, and treatment burdens across all age groups (Behan et al., 2017a). Lung function, pulmonary exacerbations, and body mass index all affected QOL scores in children with respiratory illness. Treatments including oral azithromycin, nebulized antibiotics, all forms of ACT, pulmonary rehabilitation, and other exercises have all shown some improvement in QOL scores (Nathan et al., 2017).

2.2 Similar studies

PCD is a rare condition with multisystem involvement. Despite the lack of evidence for the management of PCD, ensuring early diagnosis and a multidisciplinary team approach can assist patients in achieving the best possible outcomes. Regular airway clearance, including chest physiotherapy and physical exercise in patients with PCD, is important as a part of the treatment program. There is an urgent need for further research regarding PCD (Kumar & Walker, 2020; A. L. Lee et al., 2015a).

Chest physiotherapy technique prescription with children or adolescents is variable. Technique selection and prescription should be individualized, according to age and specific patient adherence (A. L. Lee et al., 2017).

The ACBT is the most often utilized bronchial hygiene therapy for reducing inflammation and infection while also enhancing lung function by eliminating secretions. The flutter device is a small portable device with a steel ball inside a cone. As the steel ball is displaced, an oscillating pressure wave is created. This positive expiratory pressure helps to release secretions, prevent bronchial closure, and mobilize sputum. Studies showed that both ACBT and the flutter device demonstrate considerable improvements in treating bronchiectasis patients, although they are equally effective when compared (Athawale et al., n.d.; Thompson et al., 2002). In another study, flutter devices and ACBT were found to be effective home-based physiotherapeutic treatments. The flutter device's higher efficacy in certain parameters could be linked to its ease

of use and subsequent increases in treatment compliance. The flutter device appears to be more efficient in terms of sputum output (Üzmezoğlu et al., 2018).

The Acapella is another portable device that provides oscillation to the airways, which aids in the loosening and centralization of secretions. OPEP devices produce pressure by a one-way valve that allows for free inspiration while resisting expiration with oscillations. These oscillations are thought to cause vibrations within the airway wall, causing secretions to be displaced. According to studies, acapella is just as safe and effective as traditional chest physiotherapy, or ACBT. It is favored by the majority of patients. Patients found acapella to be a more comfortable, user-friendly device that can be used independently. Therefore, it may be a feasible and alternative chest physiotherapy treatment option for PCD patients (Bingol et al., 2020; Patterson et al., 2005).

Additionally, a related study recommended that the Aerobika OPEP device should be employed in the postoperative setting as a beneficial addition to the standard of care (Burudpakdee et al., 2018). Sahardin et al showed that using Aerobika significantly improved lung function, 6MWT, and COPD assessment test scores, in COPD patients (Sahardin et al., 2023a). The Aerobika device is a cost-effective treatment option for patients with COPD (Khoudigian-Sinani et al., 2017).

Evidence suggests that OPEP therapy improves sputum expectoration in non-CF bronchiectasis patients when compared to no treatment. It may also be equally effective as other ACTs. Lung hyperinflation measurements have been demonstrated to be reduced with OPEP therapy. Short-term treatment with the Acapella or the Flutter is suggested over alternative approaches. In individuals with non-CF bronchiectasis, a longer-term trial is needed to compare OPEP treatment to other ACTs (A. L. Lee et al., 2015).

Another ACT method, the mechanical chest percussion (MP), this machine simulates the therapist's manual clapping. It allows the patient by himself to establish his or her percussion frequency and intensity. In patients with lower respiratory tract infections, OPEP was more effective than MP in draining sputum, improving oxygenation, and reducing inflammatory state; however, it did not affect microbial clearance (Ni et al., 2018).

Different types of ACTs, such as the active cycle of breathing technique, autogenic drainage, forced expiration technique, postural drainage, high-frequency chest wall oscillation, oscillating positive expiratory pressure, and exercise or pulmonary rehabilitation, appear to be safe for patients (adults and children) with stable bronchiectasis; in which important clinical outcomes such as sputum expectoration, selected measures of lung function, exercise or pulmonary rehabilitation, and quality of life may be improved (Nathan et al., 2017).

3. Chapter three: Methods and procedures

3.1 Study design

3.2 Study setting

3.3 Study sample

3.4 Data collection

3.5 Study procedure

3.6 Statistical analysis

3.7 Ethical considerations

3.1 Study design

It is an experimental study that included pre-, mid-, and post-tests. Using an experimental methodology was suitable for this study to compare the effectiveness of the applied interventions on lung function, functional exercise capacity, quality of life and activities of daily living among PCD patients.

3.2 Study Setting

The participants were pediatric patients with PCD from West Bank, Palestine. They were treated as in or outpatients in Caritas Baby Hospital- Bethlehem. Participants were trained and followed up in the same hospital. Participants performed the required intervention as home-based treatment sessions.

3.3 Study sample

3.3.1 Sampling method

The sample was selected through stratified randomized sampling. The stratification was done according to age categories (6–12 years old and 13–18 years old). Patients were assigned randomly by simple randomization using an Excel sheet, with even numbers allocated to the ACBT arm (n = 16) and odd numbers to OPEP (n = 16).

3.3.2 Sample size

A total of 48 PCD participants, male and female, were recruited in this experimental study from our database, ages ranging from 6 to 18 years. 32 pediatric patients with PCD were enrolled in the study as they met the inclusion criteria (Fig. 3.1). Based on the global prevalence of PCD (1/10000) and the absence of prevalence studies on PCD in Palestine, the number is expected to be adequate to achieve the study objectives.

3.3.3 Inclusion criteria

- Subject with the diagnosis of PCD, confirmed by either transmission electron microscopy and/or positive genetic testing.
- Subjects living in the West Bank, Palestine
- Age ranged from 6 to 18 years old
- Subjects who were clinically stable
- Oriented and able to carry out their chest physiotherapy home program by themselves or with assistance from parents.
- Parents were willing to sign a consent form.

3.3.4 Exclusion criteria

- Pneumothorax within 1 year of study commencement.
- Subjects with a history of significant hemoptysis.
- Subjects with chest trauma.
- Subjects with other chronic or respiratory diseases such as heart disease, asthma, etc…
- Subjects with delay cognitive abilities.
- Subjects who were unable to undertake pulmonary function testing (PFTs).
- Parents refused their children to participate in the study.

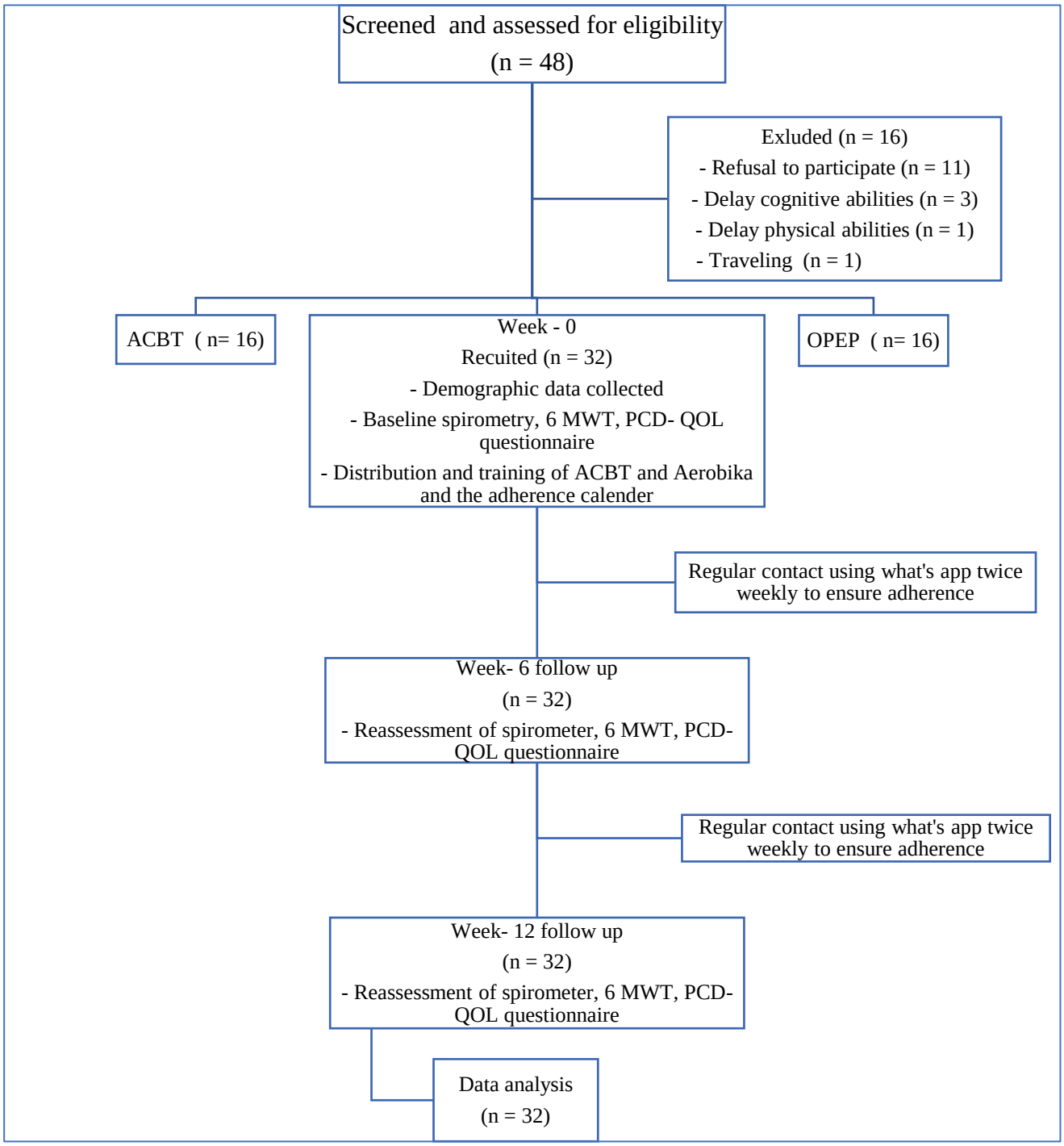

Figure 3.1 Study design and flow of participants through the study

3.4 Data collection

Tools of data collection

- A data collection sheet was formed by the physiotherapist (Appendix 1). This contains personal data (patient's code, gender, age, and address), patient's medical history, medications, sputum culture, cough, sputum characteristics, and other associated symptoms such as headaches, hearing problems, nasal congestion, voice changes, chest pain, and clubbed fingers.
- Body mass index (BMI): an index that uses a person's weight and height to calculate body fat in males and females of any age. It's computed by dividing a person's weight in kilos by their squared height in meters (Weir & Jan, 2019).
- Spirometry: It is the most common pulmonary function test, it is considered a valid and reliable test for assessing lung function when conducted under standardized guidelines (Moore, 2012). Spirometer is widely used in the measurement of lung function to offer objective data for lung disease diagnosis and monitoring. Spirometry is a physiological test that determines the maximum amount of air a person can inhale and exhale while performing maximum effort. In spirometry, the basic signal is either volume or flow as a function of time.

  The most important readings in obstructed lung disease are the forced vital capacity (FVC) and forced expiratory volume in the first second (FEV_1) (Miller et al., 2014). The FVC is the volume delivered during a forceful and complete expiration beginning with full inspiration, and the FEV_1 is the expiratory volume delivered in the first second of the FVC. Spirometry is an important tool for determining general respiratory health. It can be used to assess airway responsiveness, monitor disease progression or the effectiveness of therapeutic interventions, assess preoperative risk, and determine a prognosis for a variety of pulmonary disorders (Graham, Steenbruggen, Miller, et al., 2019).
- Six-Minute Walk Test (6MWT) (Appendix 2): is a valid and reliable test that can help in assessing the functional exercise capacity of patients with cardiopulmonary disease (Spruit et al., 2012).It is a reliable and valid test. The 6MWT has been recommended by the American Thoracic Society (ATS) as an effective outcome measure in clinical trials (Holland et al., 2014).

- Pulse oximetry is a non-invasive measurement of Oxygen saturation that calculates the percentage of oxygenated hemoglobin in the blood. Pulse oximetry is a simple, valid and reliable procedure that is both relevant and repeatable over time (Lauwers et al., 2020).
- Quality of life questionnaire for primary ciliary dyskinesia (PCD- QOL Questionnaire) (Arabic version) (Appendix 3):

  For this study, a quality-of-life questionnaire was designed by the researcher based on previous studies (Al-Moamary et al., 2011; Alyami et al., 2015). The questionnaire consists of three domains with 15 items: 5 items concerning daily activities, 5 items concerning physical functioning, and 5 more items related to social and school functioning. The questionnaire is based on a 3-point Likert-type scale (with possible responses of: Never=3, Sometimes=2, and Always=1). The questionnaire was validated by 6 experts in the field. In addition, a pilot study was conducted with 10 patients with PCD (6-18 years) to verify if all questions were understandable. Accordingly, some minor modifications were performed.
- A monthly calendar (Appendix 4): to ensure and monitor adherence to the prescribed home program was designed, and each participant was provided with a monthly calendar. The participants were instructed to mark the completion of the home program (the nebulization's and the ACT) with a tick twice a day (Fig. 3.2).

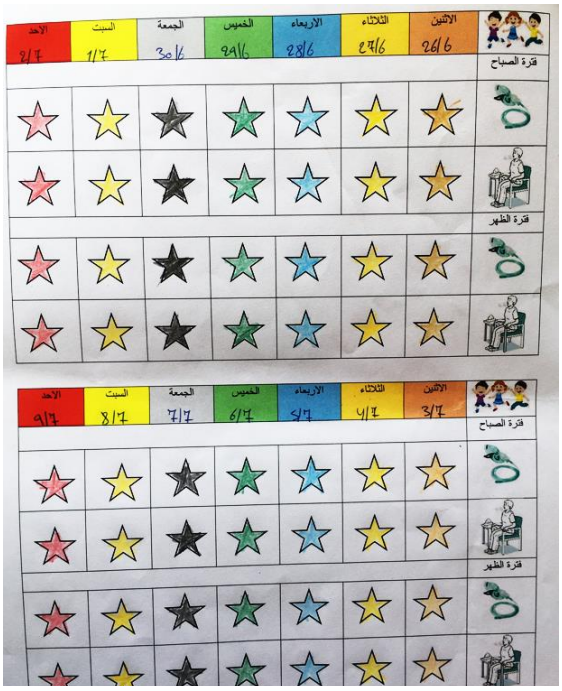

Figure 3.2 An example of the monthly calendar

Study procedures

The study took place at Caritas Baby Hospital after receiving ethical approval from the research committee of the hospital. Participants with a PCD diagnosis were recruited from the database of Caritas Baby Hospital-Bethlehem. Before beginning the study, all participants underwent a familiarization training session in the hospital to be independent in performing ACBT or OPEP. The intervention took three months to be completed between June 2023 to October 2023. The participants were asked to perform two sessions daily at home, each session took around 15 minutes. The therapist monitored and observed the procedure twice weekly by contacting the participant via WhatsApp. Participants received encouraging messages and emojis to help them stay focused on the program (Fig. 3.3).

Figure 3.3 An example of encouragement emojis that were sent to participants via WhatsAPP

It was important to make sure that home medications (inhaled or oral antibiotics, bronchodilators, hypertonic saline, and supplements) were continued unchanged during the time of the study.

Daily adherence to ACT, nebulizers, and any medications that were administered during the study period were recorded in the designed calendar.

3.5 Suggested program

Two weeks before the intervention the patients received a training session. They were all fully trained in the method that they would apply. A baseline pre-test was conducted by an independent assessor who was blinded to the treatment order. The blinded assessor is a qualified physiotherapist. Before attending the clinic appointment, participants were asked to wear comfortable clothing and shoes. As part of the baseline pre-test, height, weight, and BMI were recorded for each participant. The data collection sheet and the PCD-QOL

questionnaire were completed. Spirometry was used to measure lung function as illustrated in (Fig. 3.4). Data collected comprised the FEV_1 (in liters and % predicted), the FVC (in liters and % predicted), the FEV_1/FVC ratio, and the maximal -expiratory flow $MEF_{25-75\%}$. Spirometry was performed using Smart PFT Lab TM (Medical Equipment Europe GmbH, Hammelburg, Germany). The American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines were followed when performing a spirometry test.

Furthermore, the functional exercise capacity was assessed by the distance a participant can walk in 6 minutes according to the ATS guidelines of 6MWT as illustrated in (Fig 3.5). Before starting a 6MWT, each participant would need to check and record their heart rate (HR), blood pressure (BP), pulse oximetry (SpO2), and rate their dyspnea and overall fatigue using the Modified Borg scale while they were resting. Following the 6-minute walk test, HR, SpO2, dyspnea, and fatigue rates were reassessed and recorded. The test was conducted on a 30-meter-long straight corridor, marked every 3 meters. Participants were given verbal instructions to walk as far as they could without running or jogging for six minutes.

During week 6 and week 12, participants were followed up and performed a reassessment of the outcome measures that were conducted by the same blinded assessor to prevent the assessor's bias.

Figure 3.5 Illustration of performing a spirometry test

Figure 3.4 Illustration of performing a 6 MWT

On each day of the intervention, the patients were asked to perform two sessions of ACT-morning and evening, before meals. If subjects routinely used bronchodilators and hypertonic saline nebulizers, they were administered before the treatment session. Patients were requested to be compliant with the suggested program and record the treatment they received in their monthly calendar.

Group 1: ACBT

ACBT (Fig. 3.6) was applied with its three phases as a cycle of breathing control (20-30 sec.), thoracic expansion exercises (five times), breathing control, thoracic expansion exercises (five times), breathing control, and forced expiration technique (Huffing then cough).

This technique was performed in a sitting position.

The duration of ACBT lasted for 15-20 minutes.

Figure 3.6 Illustrating ACBT performance: (A) Breathing control, (B) Thoracic expansion, (C) Huffing.

Group 2: OPEP

Instructions for the use of the OPEP device (Fig. 3.7):

- The patient should be well seated.
- The patient should place the mouthpiece of the device in the mouth and close the lips firmly to ensure an effective seal.
- Through the mouthpiece, the patient was instructed to breathe slightly larger than the tidal volume.
- The patient was then instructed to hold breath for 2–3 seconds.
- A slight active expiration was then performed through the OPEP mouthpiece. It is recommended to exhale 3–4 times longer than the inhalation taken.
- A typical cycle of OPEP therapy consists of 10–20 breaths through the device.
- Following the previous cycle, the forced expiration technique was used, followed by coughing to further mobilize secretions.

Figure 3.7 Illustrating Aerobika therapy

· The treatment period lasted for 15-20 minutes.

3.6 Statistical analysis

Data was analyzed using descriptive statistics and inferential statistics using means, medians, and ranges. Statistical analysis was performed via the Statistical Package for the Social Sciences (SPSS) package, version 26 (SPSS Inc., Chicago, IL). Descriptive statistics were performed to characterize the sample according to age, sex, clinical manifestations, and other variables. T-Tests and ANOVA were performed on parametric variables such as spirometry measures and the 6MWT to determine differences between the two groups in pre, mid, and posttests. The effect size was calculated using Cohen's d. In addition, correlation tests (Pearson's and Spearman's tests) were performed to determine the association between the studied variables. Statistical significance was set at p-value < 0.05.

3.7 Ethical considerations

Ethical approval was obtained from the Research Ethical Committee of Al-Quds University (Appendix 5), and the Research Ethical Committee of Caritas Baby Hospital- Palestine (Appendix 6). The scope and aim of the study were clearly explained to the children participating in the study and their families. Written informed consent was obtained from the guardians (Appendix 7).

4. Chapter four: Result and discussion

4.1 Result presentation and analysis

4.2 Result discussion

4.3 Study limitations

4.1 Result presentation and analysis

4.1.1 Descriptive statistics

4.1.1.1 Demographic data for the participants

A total of 32 participants with a mean age of 11.09± 3.26 met the inclusion criteria and were recruited between June 2023 and October 2023, with 16 participants in each of the ACBT and OPEP groups. All 32 completed the study. Participants were categorized into two age groups (6-12 years and 13-18 years) and were distributed equally in both groups of intervention. Demographic characteristics are illustrated in Table (4.1).

Table 4.1 Demographic characteristics of the participants

Baseline characteristics	ACBT	OPEP
Subjects (n)	16	16
Age years (mean± SD)	10.94± 3.54	11.25± 3.06
Age categories		
6-12 years	10	10
13-18 years	6	6
Sex (n)		
Male	8	11
Female	8	5

4.1.1.2 Descriptive statistics related to anthropometry measurements

Measurements of weight, height, and BMI in the two groups didn't show statistical significance ($p > 0.05$) as shown in Table (4.2)

Table 4.2 Anthropometric measurements of the participants (n=32)

Variables	ACBT (n=16)	OPEP ACBT (n=16)	p- value
Weight kg (mean± SD)	36.87± 14.51	42.68± 17.00	0.31
Height m (mean± SD)	1.38± 0.24	1.46± 0.19	0.31
BMI kg/m^2 (mean± SD)	18.68± 3.54	19.07± 4.18	0.77

4.1.1.3 Descriptive statistics related to parental consanguinity

A total of 28 (87.5%) of the study population have a positive history of parental consanguinity as shown in Figure (4.1). Thirteen families from the recruited groups have siblings with PCD.

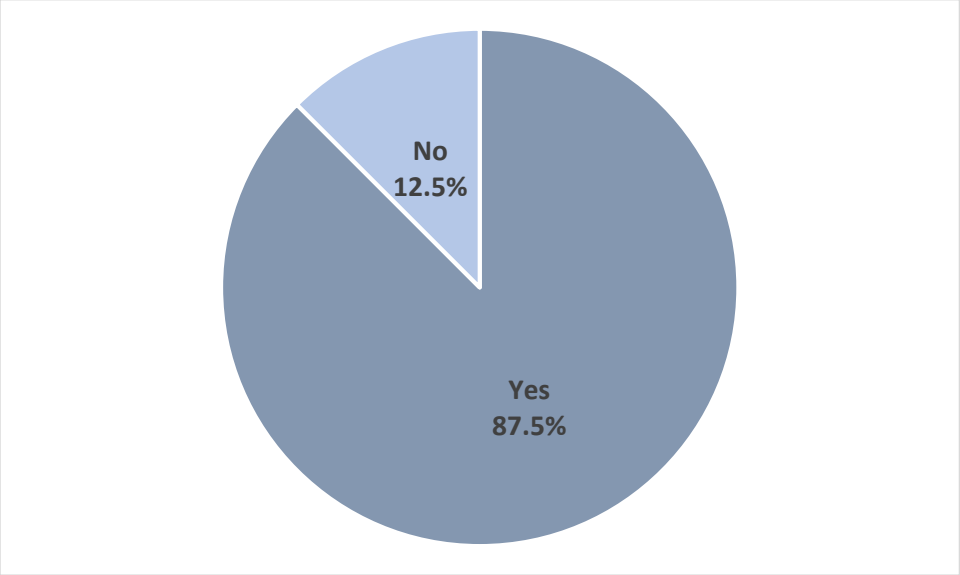

Figure 4.1 Parental consanguinity in the study population (n=32)

4.1.1.4 Descriptive statistics related to the geographic distribution of the participants

The majority of participants were from Hebron, constituting 57.4% of the study population. Bethlehem followed, with 15.6% representation, while Ramallah accounted for 9,4%. Participants from other cities represented 12.4% as illustrated in (Table 4.3) and (Fig 4.2).

Table 4.3. Address distribution of the participants (n=32)

Address	Frequency	Percent
Hebron	19	57.4%
Bethlehem	5	15.6%
Ramallah	3	9.4%
Tubas	2	6.3%
Jerusalem	1	3.1%
Jenin	1	3.1%
Qalqilya	1	3.1%

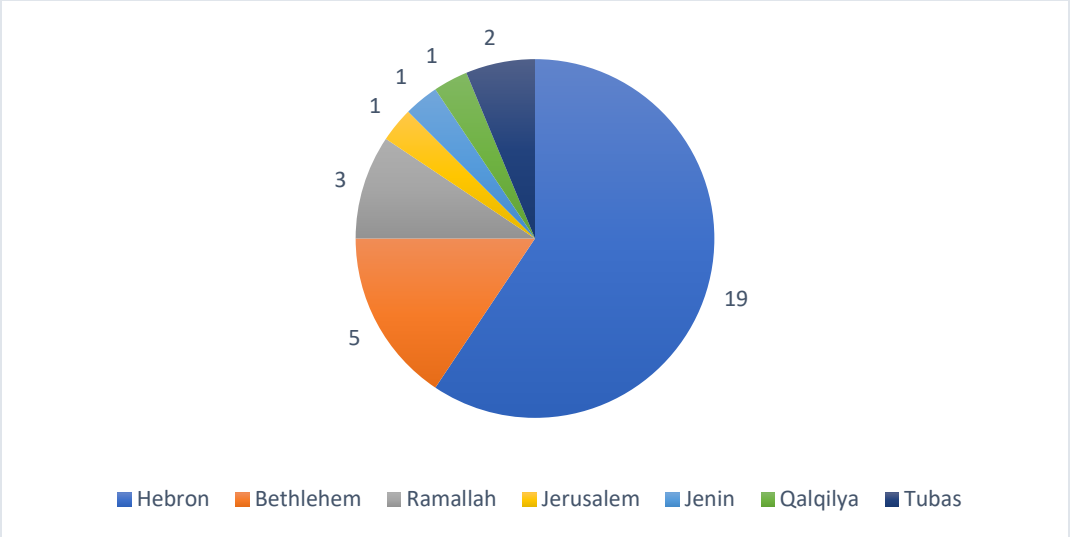

Figure 4.2 Address distribution of the participants (n=32)

4.1.1.5 Descriptive statistics related to the clinical features of the participants

The prevalence of clinical features among the study participants in the last 3 weeks indicates the majority of 84.4% reported nasal congestion. Half of the participants reported hearing problems, and chest pain, 37.5% complained of headache, 34.4% experienced changes in voice, and 18.8% reported fever as illustrated in (Table 4.4).

Table 4.4. Clinical features of the participants (n=32)

Clinical features	Frequency	Percent
Headache		
Yes	12	37.5%
No	20	62.5%
Hearing problems		
Yes	16	50%
No	16	50%
Nasal congestion		
Yes	27	84.4%
No	5	15.6%
Voice changes		
Yes	11	34.4%
No	21	65.6%
Fever		
Yes	6	18.8%
No	26	81.3%
Chest pain		
Yes	16	50%
No	16	50%
Clubbing fingers		
Yes	6	18.8
No	26	81.3%

4.1.1.6 Descriptive statistics related to cough, sputum characteristics, and sputum culture

The majority of participants 90.6% reported a productive cough, while wheezy and dry cough characteristics were less common. In addition, 75% reported a viscous sputum consistency. In terms of sputum color, participants reported yellow 46.9%, green 37.5%, and clear 15.6% as shown in (Table 4.5).

Table 4.5 Cough and sputum characteristics (n=32)

	Frequency	Percent
Cough characteristics		
Productive	29	90.6%
Wheezy	2	6.3%
Dry	1	3.1%
Sputum consistency		
Viscous	24	75%
Thick	4	12.5%
Thin	4	12.5%
Sputum color		
Yellow	15	46.9%
Green	12	37.5%
Clear	5	15.6%

Regarding the sputum culture results taken in the last 6 months, the most prevalent sputum culture in ACBT was “normal” (43.8%) and “Haemophilus influenzae” 37.5%, while in OPEP “Haemophilus influenzae” 37.5% and “normal” 25% were the most common. Staphylococcus aureus and others had lower percentages as shown in (Table 4.6) and (Fig. 4.3).

Table 4.6 Sputum culture taken in the last 6 months

	ACBT (n=32)		OPEP (n=32)	
	Frequency	Percent	Frequency	Percent
Normal	7	43.8%	4	25%
Haemophilus influenzae	6	37.5%	6	37.5%
Haemophilus parainfluenzae	1	6.3%	0	0%
Pseudomonas aeruginosa	1	6.3%	1	6.3%
Staphylococcus aureus	4	25%	3	18.8%
Staphylococcus aureus MRSA	1	6.3%	2	12.5%
Streptococcus pneumoniae	0	0%	1	6.3%

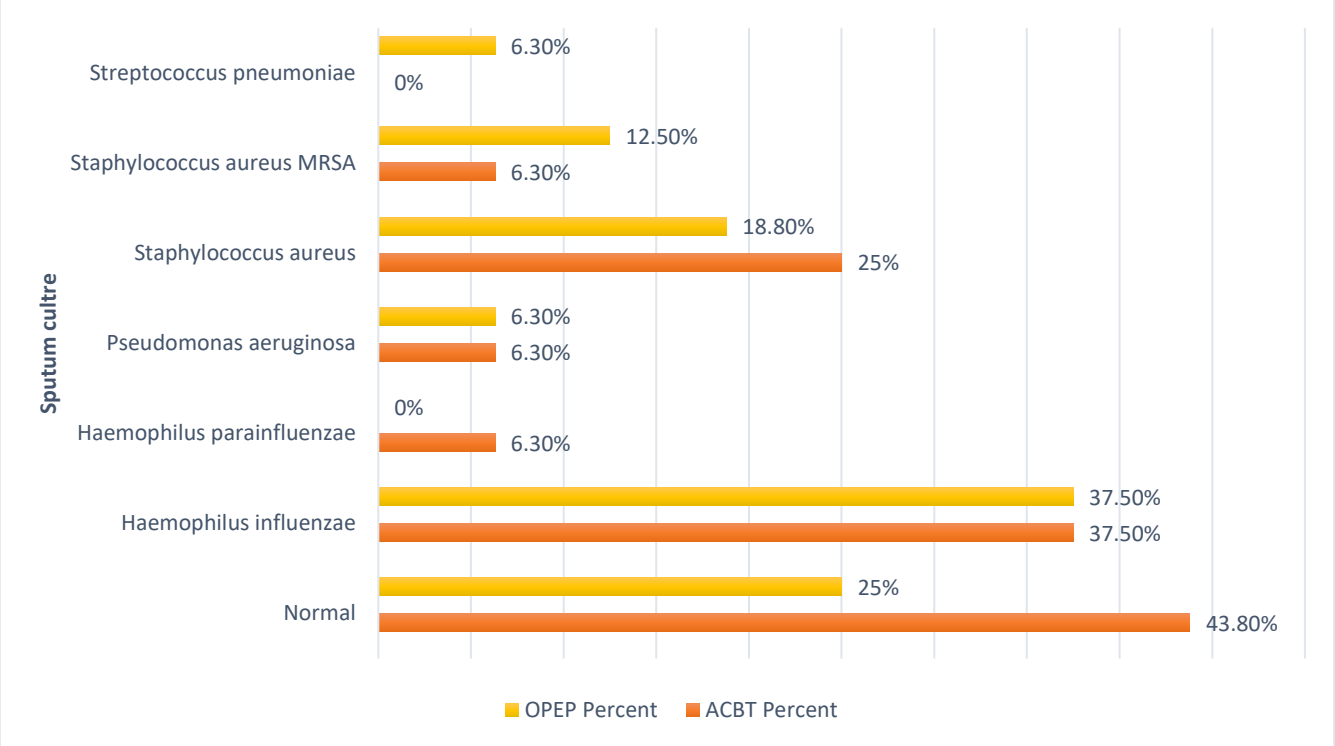

Fig. 4.3 Sputum culture in the two groups of the population (n-32)

4.1.1.7 Descriptive statistics related to spirometry

The mean difference between the two groups of lung function tests including FEV_1, FVC, FEV_1/FVC, and the $MEF_{25-75\%}$ showed no statistical significance ($p > 0.05$). Table (4.7) demonstrates the descriptive statistics of the Spirometry parameters.

Table 4.7 Baseline spirometry parameters

	ACBT (n=16)				OPEP (n=16)				P-value
	Mean	SD	Median	Min-Max	Mean	SD	Median	Min-Max	
FEV_1 $\%_{predicted}$	78.18	22.71	83.0	36- 109	86.56	18.12	89.0	44- 110	0.25
FVC $\%_{predicted}$	74.87	23.89	81.5	31- 104	85.81	19.69	87.5	40- 118	0.16
FEV_1/FVC %	90.06	8.63	91	73- 100	85.56	6.59	84.5	76- 100	0.10
$MEF_{25-75\%}$ $\%_{predicted}$	79.62	25.88	72.50	49- 139	82.31	24.34	85.0	34- 123	0.76

4.1.1.8 Descriptive statistics related to the 6-minute walk test

The results of the mean distance of the 6 MWT test in the ACBT and the OPEP were 428.26± 62.6 and 448.91± 53.4, respectively. There was no statistical significance ($p > 0.32$) as illustrated in (Table 4.8).

Table 4.8 Baseline 6 MWT measured in meter

ACBT (n=32)				OPEP (n=32)				P- value
Mean	SD	Median	Min-Max	Mean	SD	Median	Min-Max	
428.26	62.66	429.0	336.30- 598.50	448.91	53.48	441.0	340.50- 552.0	0.32

4.1.1.9 Descriptive statistics related to the PCD QOL questionnaire

Table (4.9) illustrates the results of the 15 questions of the 3-point Likert-type scale questionnaire (with possible responses of: Never, Sometimes, and Always) for both groups.

Table 4.9 Baseline PCD QOL questionnaire frequency response in each group (n=32)

	Never		Sometimes		Always	
	ACBT	OPEP	ACBT	OPEP	ACBT	OPEP
Q1. How often did coughing affect your daily life?	1	2	9	12	6	2
Q2. How uncomfortable was your cough during the day?	3	2	6	10	7	4
Q3. How easily did you feel fatigued by the cough?	2	2	11	10	3	4
Q4. How often was your sleep affected by your breathing problem?	6	9	5	2	5	5
Q5. How often did your breathing problem affect your daily activities at home?	12	13	1	1	3	2
Q6. Walking	8	9	5	5	3	2
Q7. Climbing stairs	6	9	5	3	5	4
Q8. Carrying things	9	9	5	5	2	2
Q9. Running	1	3	10	9	5	4
Q10. Exercising and sport	2	5	10	8	4	3
Q11. Talking	9	10	5	5	2	1
Q12. Playing with children/ pets	12	14	3	2	1	0
Q13. Visiting friends/ relatives	12	13	4	3	0	0
Q14. How often did it affect your school attendance?	11	13	5	3	0	0
Q15. How often did it affect your performance in school?	13	13	2	3	1	0

Table (4.10) demonstrates the descriptive statistics of the three items of the questionnaire with its total score. The mean difference of the total score of ACBT was 33.75± 5.17 and 35.81± 6.27 for the OPEP. P value was > 0.05 in all of the items and in the total score, there was no statistical significance.

Table 4.10 Baseline PCD QOl items and total score

	ACBT (n= 16)			OPEP (n= 16)			p-value
	Mean	SD	Median	Mean	SD	Median	
Q. 1-5 Daily activities	10.0	2.60	10.50	10.68	2.41	11.0	0.44
Q. 6-10 Physical functioning	10.43	2.94	11.0	11.25	3.19	13.0	0.46
Q. 11-15 Social and school functioning	13.31	1.85	13.50	13.87	1.54	14.50	0.35
Total score	33.75	5.17	33.50	35.81	6.27	37.50	0.31

4.1.1.10 Normality of the data distribution of the main dependent variables

A normality distribution test of the dependent variables of the study was conducted before data analysis. For this, the Kolmogorov- Smirnov Z test was employed. The majority of the study variables showed a statistical significance of the normality tests ($p > 0.05$), this allows the use of parametric statistical methods. Normality tests are illustrated in (Table 4.11)

Table 4.11 Tests of Normality for the main dependent variables in the study

	Kolmogorov-Smirnov			Shapiro-Wilk		
	Statistic	Df	Sig.	Statistic	df	Sig.
FEV_1- Pre	.17	32.00	.02	.93	32.00	.04
FVC- Pre	.18	32.00	.01	.91	32.00	.01
FEV_1/FVC- Pre	.09	32.00	.20*	.96	32.00	.23
$MEF_{25-75\%}$- Pre	.08	32.00	.20*	.98	32.00	.79
6 MWT- Pre	.13	32.00	.20*	.95	32.00	.18
PCD- QOL- Pre	.14	32.00	.09	.95	32.00	.11
FEV_1- Mid	.16	32.00	.05	.94	32.00	.08
FVC- Mid	.10	32.00	.20*	.97	32.00	.38
FEV_1/FVC- Mid	.12	32.00	.20*	.95	32.00	.12
$MEF_{25-75\%}$- Mid	.10	32.00	.20*	.98	32.00	.69
6 MWT- Mid	.11	32.00	.20*	.99	32.00	.96
PCD- QOL- Mid	.24	32.00	.00	.80	32.00	.00
FEV_1- Post	.15	32.00	.08	.96	32.00	.22
FVC- Post	.10	32.00	.20*	.96	32.00	.23
FEV_1/FVC- Post	.08	32.00	.20*	.96	32.00	.27
$MEF_{25-75\%}$- Post	.11	32.00	.20*	.97	32.00	.54
6 MWT- Post	.10	32.00	.20*	.98	32.00	.70
PCD- QOL- Post	.23	32.00	.00	.82	32.00	.00

*. This is a lower bound of the true significance.

4.1.2 Interferential statistics

4.1.2.1 Baseline interferential statistics for the main dependent variables

At baseline, there was no statistical significance between the main dependent variables and sex group (male, female) p> 0.05 as shown in (Table 4.12).

Table 4.12 Baseline inferential statistics between sex and study variables

	Sex	Mean	Std.	Std. Error	p-value
$FEV_1\%_{Pred}$	Male	81.84	17.86	4.10	0.86
	Female	83.15	24.96	6.92	
$FVC\%_{Pred}$	Male	79.68	18.43	4.23	0.84
	Female	81.31	27.70	7.68	
$FEV_1/FVC\%$	Male	86.79	8.07	1.85	0.38
	Female	89.31	7.70	2.13	
$MEF_{25-75}\%_{Pred}$	Male	80.42	26.69	6.12	0.88
	Female	81.77	22.65	6.28	
6 MWT	Male	438.80	50.44	11.57	0.98
	Female	438.29	70.37	19.52	
PCD- QOL	Male	34.16	6.02	1.38	0.47
	Female	35.69	5.44	1.51	

Regarding age category, there was no statistical significance between the main dependent variables and age category (6-12 years, 13-18 years) p>0.05 as shown in (Table 4.13).

Table 4.13Baseline inferential statistics between sex and study variables

	Age	Mean	Std.	Std. Error	p-value
$FEV_1\%_{Pred}$	6-12	78.65	21.96	4.91	0.19
	13-18	88.58	17.40	5.02	
$FVC\%_{Pred}$	6-12	76.75	23.09	5.16	0.24
	13-18	86.33	20.28	5.85	
$FEV_1/FVC\%$	6-12	88.30	8.89	1.99	0.66
	13-18	87.00	6.18	1.78	
$MEF_{25-75}\%_{Pred}$	6-12	77.70	27.27	6.10	0.34
	13-18	86.42	19.76	5.70	
6 MWT	6-12	433.70	59.66	13.34	0.55
	13-18	446.74	57.46	16.59	
PCD- QOL	6-12	34.40	6.12	1.37	0.64
	13-18	35.42	5.28	1.52	

4.1.2.2 Spirometer interferential statistics

4.1.2.2.1 The mean difference of the FEV_1 between the two groups

There was no statistically significance difference in the FEV_1 between the two groups in the pre-test $p > 0.05$. Conversely, there was a statistically significant $p < 0.05$ for the mean differences in FEV_1 between the mid and post-tests as shown in (Table 4.14) and (Fig.4.4). In the post-test, the OPEP demonstrated a greater improvement in the FEV_1 parameter with a large effect size of Cohen's d= 0.86.

Table 4.14 The mean difference of the $FEV_1\%_{Pred}$ between the two groups (n= 32)

		Mean	Std. Deviation	Std. Error	P-value	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
FEV_1- Pre	ACBT	78.18	22.71	5.67	0.25	66.08	90.29	36.00	109.00
	OPEP	86.56	18.12	4.53		76.90	96.22	44.00	110.00
FEV_1- Mid	ACBT	83.37	21.82	5.45	0.05	71.74	95.00	49.00	112.00
	OPEP	96.50	13.55	3.38		89.27	103.72	73.00	129.00
FEV_1- Post	ACBT	80.81	20.38	5.09	0.02	69.95	91.67	46.00	106.00
	OPEP	96.00	14.27	3.56		88.39	103.60	75.00	125.00

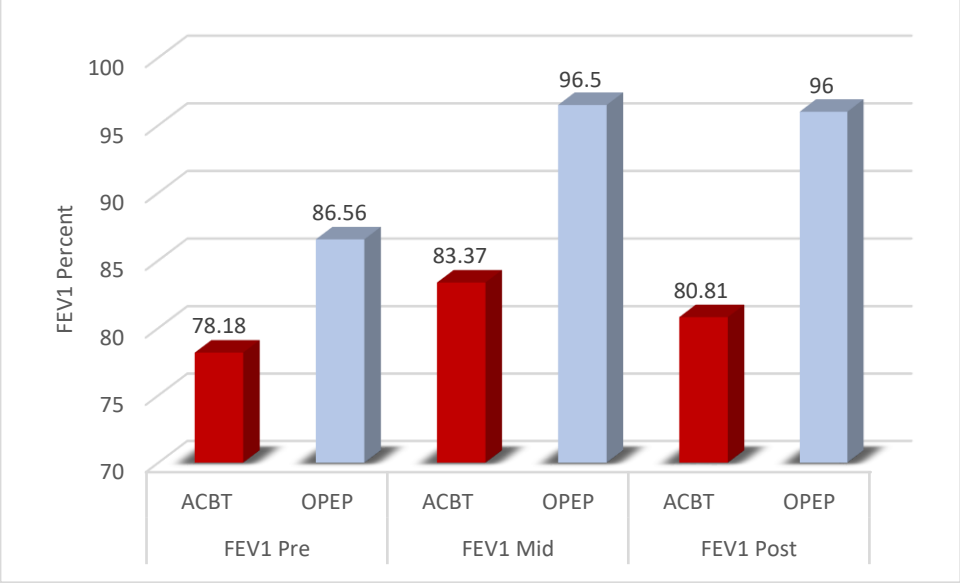

Figure 4.4 FEV_1 percentage between both groups during the intervention (n= 32)

4.1.2.2.2 The mean difference in the FVC between the two groups

The result showed that there was no statistical significance in both groups in the pre-, mid, and post-tests p> 0.05 as illustrated in (Table 4.15). In the post-test, there was a moderate Cohen's d= 0.68.

Table 4.15 The mean difference of the FVC%$_{Pred}$ between the two groups (n= 32)

		Mean	Std. Deviation	Std. Error	P- value	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
FVC Pre	ACBT	74.88	23.89	5.97	0.16	62.14	87.61	31.00	104.00
	OPEP	85.81	19.70	4.92		75.32	96.31	40.00	118.00
FVC Mid	ACBT	80.19	22.66	5.67	0.07	68.11	92.26	43.00	114.00
	OPEP	93.38	16.70	4.17		84.48	102.27	62.00	124.00
FVC Post	ACBT	79.31	22.83	5.71	0.06	67.15	91.48	40.00	110.00
	OPEP	92.81	16.32	4.08		84.12	101.51	63.00	119.00

4.1.2.2.3 The mean difference of the FEV_1/FVC in the two groups

Table (4.16) illustrates the mean difference of the FEV_1/FVC in the two groups. There was no statistical significance between the two groups. Cohen's d= 0.03 in posttest.

Table 4.16 The mean difference of the FEV_1/FVC% between the two groups (n= 32)

		Mean	Std. Deviation	Std. Error	P-value	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
FEV_1/FVC- Pre	ACBT	90.06	8.64	2.16	0.10	85.46	94.66	73.00	100.00
	OPEP	85.56	6.59	1.65		82.05	89.08	76.00	100.00
FEV_1/FVC- Mid	ACBT	89.44	8.37	2.09	0.43	84.98	93.90	74.00	100.00
	OPEP	87.38	6.33	1.58		84.00	90.75	75.00	100.00
FEV_1/FVC- Post	ACBT	88.06	9.55	2.39	0.91	82.98	93.15	71.00	100.00
	OPEP	87.75	6.92	1.73		84.06	91.44	74.00	100.00

4.1.2.2.4 The mean difference of the $MEF_{25-75\%}$ in the two groups

The mean difference between the two groups $MEF_{25-75\%}$ is shown in (Table 4.17). Only in the post-test, there was a statistically significant difference between the groups ($p<0.05$), where the mean score of the OPEP was higher 95.38± 21.49; in the pre-and mid-tests, there was no statistical significance (p.0.05). In the post-test, the OPEP demonstrated improvement in the $MEF_{25-75\%}$ parameter with a medium effect size of Cohen's d= 0.76.

Table 4.17 The mean difference of the $MEF_{25-75}\%_{Pred}$ between the two groups (n= 32)

		Mean	Std. Deviation	Std. Error	P- value	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
MEF_{25-75}- Pre	ACBT	79.63	25.88	6.47	0.76	65.83	93.42	49.00	139.00
	OPEP	82.31	24.34	6.09		69.34	95.28	34.00	123.00
MEF_{25-75}- Mid	ACBT	80.06	26.94	6.74	0.06	65.71	94.42	38.00	141.00
	OPEP	97.00	23.75	5.94		84.34	109.66	63.00	146.00
MEF_{25-75}- Post	ACBT	77.63	24.81	6.20	0.03	64.41	90.84	31.00	128.00
	OPEP	95.38	21.49	5.37		83.92	106.83	59.00	128.00

4.1.2.3 The mean difference in the 6-minute walk test

The mean difference in the total distance walked in both groups was significant only in the post-test, where the mean of the OPEP was higher than the ACBT, 486.41± 55.84 and 441.11± 69.83, respectively with the effect size of Cohen's d=0.71. Otherwise, the pre-and mid-test results showed no statistical significance as illustrated in (Table 4.18) and (Fig. 4.5).

Table 4.18 The mean difference of the 6MWT in meters between the two groups (n= 32)

		Mean	Std. Deviation	Std. Error	P-value	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
6 MWT- Pre	ACBT	428.27	62.66	15.67	0.32	394.88	461.66	336.30	598.50
	OPEP	448.91	53.48	13.37		420.42	477.41	340.50	552.00
6 MWT- Mid	ACBT	436.59	58.12	14.53	0.13	405.62	467.56	333.00	540.00
	OPEP	468.39	60.02	15.01		436.41	500.38	374.50	580.70
6 MWT- Post	ACBT	441.11	69.83	17.46	0.05	403.90	478.32	330.00	593.00
	OPEP	486.41	55.84	13.96		456.65	516.16	390.00	600.00

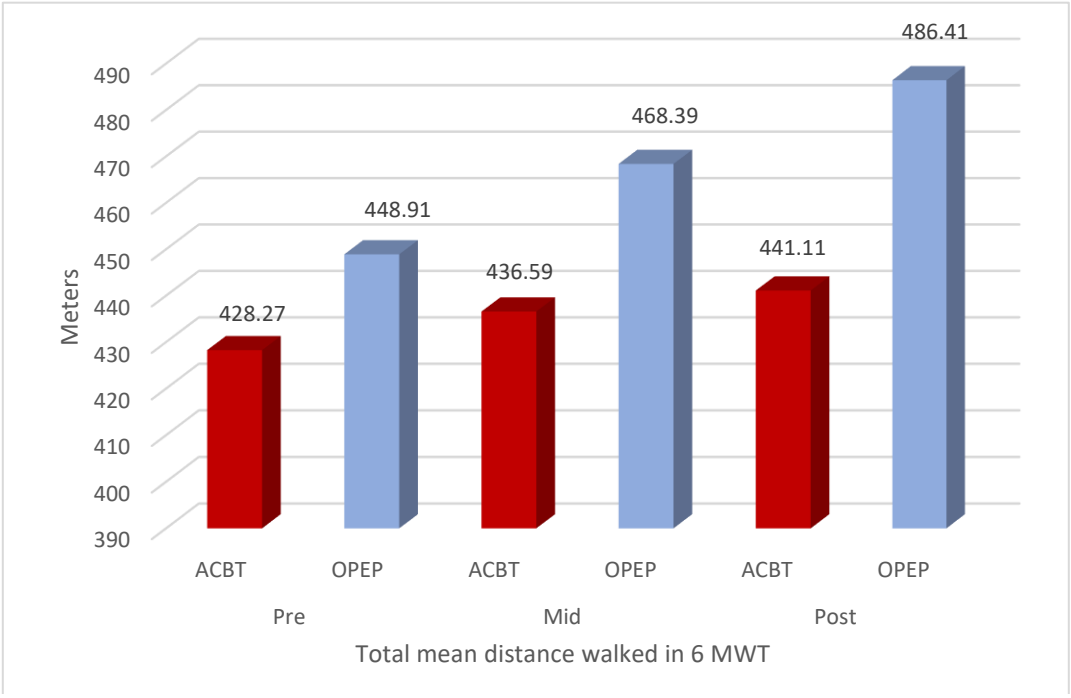

Figure 4.5 The total distance walked in meter in 6 MWT between the two groups in the intervention

4.1.2.4 The mean difference in total quality of life questionnaire results

In the overall result of the questionnaire, which was completed three times, Table (4.19) and Fig (4.6) did not reveal any statistical significance for either group ($p>0.05$). In the post-test, there was a moderate Cohen's d= 0.66.

Table 4.19 The mean difference of the total score of PCD- QOl between the two groups (n= 32)

		Mean	Std. Deviation	Std. Error	P- value	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
PCD- QOL- Pre	ACBT	33.75	5.17	1.29	0.31	30.99	36.51	24.00	40.00
	OPEP	35.81	6.27	1.57		32.47	39.16	24.00	44.00
PCD- QOL- Mid	ACBT	37.50	5.97	1.49	0.18	34.32	40.68	20.00	43.00
	OPEP	40.00	4.34	1.08		37.69	42.31	28.00	45.00
PCD- QOL- Post	ACBT	36.75	7.02	1.75	0.07	33.01	40.49	20.00	44.00
	OPEP	40.75	4.93	1.23		38.12	43.38	27.00	45.00

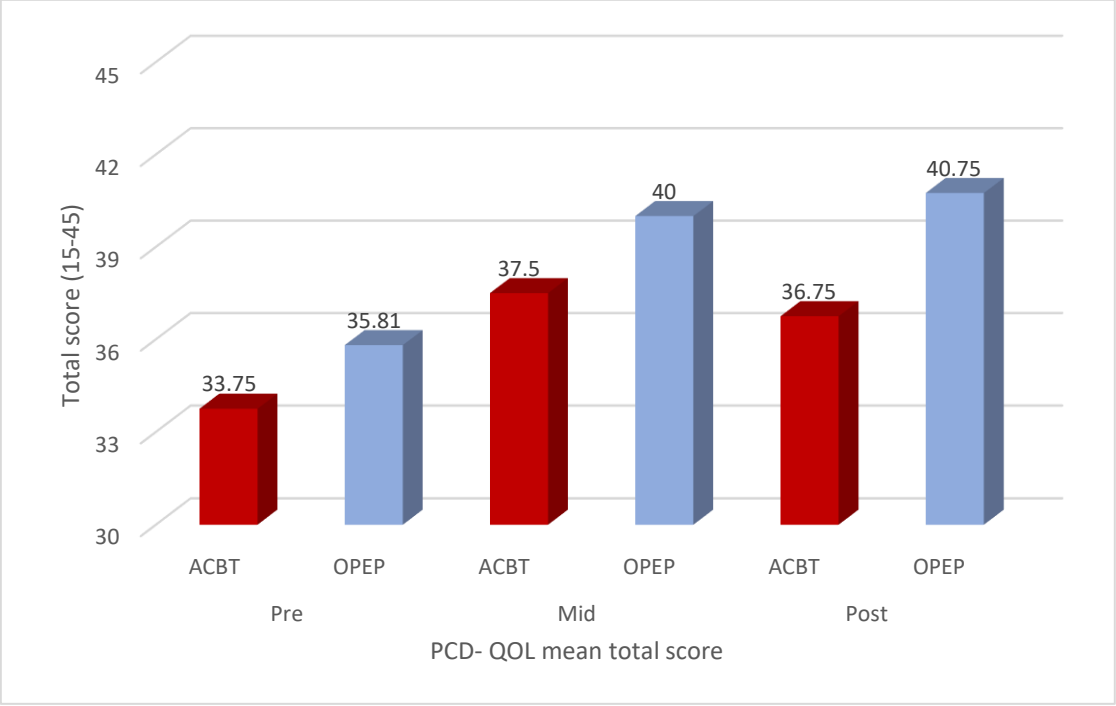

Figure 4.6 The total score of PCD- QOL between the two groups in the intervention

4.1.3 Correlations between study variables

A Pearson's correlation was conducted to determine the relationship between FEV_1, FVC, distance walked in a 6-minute walk test, and the total score of the PCD- QOL questionnaire. There was a strong, positive correlation between FEV_1 and FVC, which was statistically significant (r=0.94, p= 0.00). A moderate positive correlation between age, FEV_1, FVC, and the distance walked in a 6-minute walk test which statistically significant (r=0.53, p=0.00), (r=0.55, p=0.00), and (r=0.43, p= 0.01) respectively. Additionally, as Table (4.20) shows, there was a weak positive correlation between the total QoL questionnaire results and the walking distance.

Table 4.20 Correlation results of the outcome measures

Variables (n= 32)		Age	FEV_1	FVC	6 MWT	Total_Qol_post
Age	Pearson Correlation	1.00	.14	.19	.43*	-.07
	Sig. (2-tailed)		.44	.29	.01	.71
FEV_1	Pearson Correlation	.14	1.00	.94**	.53**	.17
	Sig. (2-tailed)	.44		.00	.00	.35
FVC	Pearson Correlation	.19	.94**	1.00	.56**	.15
	Sig. (2-tailed)	.29	.00		.00	.43
6 MWT	Pearson Correlation	.43*	.53**	.56**	1.00	.39*
	Sig. (2-tailed)	.01	.00	.00		.03
PCD- QOL	Pearson Correlation	-.07	.17	.15	.39*	1.00
	Sig. (2-tailed)	.71	.35	.43	.03	

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

4.2 Result discussion

This was the first study in Palestine comparing two different airway clearance techniques in patients with PCD. Airway clearance techniques are frequently used as a part of treatment for patients with chronic lung disease, including PCD (L. Schofield et al., 2022). Most of them complain of an increase in sputum production, and difficulty in clearing secretions that leads to chronic changes in the lung (Nielsen et al., 2022). The ACTs that are most frequently used worldwide are ACBT and OPEP therapy. Recent studies showed that ACBT is most commonly used in bronchiectasis in Europe followed by autogenic drainage (Phillips et al., 2023). On the other hand, OPEP such as Acapella, Aerobika, Flutter, and Lung flute was the most often implemented with bronchiectasis in the United States (Basavaraj et al., 2020).

In Palestine, to our knowledge, we lack the OPEP device and the important use of these devices. Our main aim was to understand the impact of two airway clearance techniques ACBT and the OPEP, on lung function, exercise functional capacity, and the PCD QOL questionnaire.

The study included a total of 32 participants age ranges from 6 to 18 years old recruited from the West Bank- Palestine. According to a recent study conducted in Palestine, 68 people were positively diagnosed with PCD; a large number of families and individuals who exhibit PCD symptoms also require further examinations (Rumman et al., 2023). In the same study, 60.3% of individuals were males, similarly, in the present study males represented 59.3% of the study population.

Regarding BMI, our study did not find a significant difference in BMI between the two groups, with a total mean of 18.87± 3.81. The observed values in both groups were within the normal range according to WHO standards for ages 5-19 years (WHO, 2023).

The majority (87.5%) of participants reported a positive history of parental consanguinity, this might be related to cultural factors, as consanguineous marriages are more common in some populations (El Goundali et al., 2022). As it is an inherited autosomal recessive disease, consanguineous marriage is related to an increased risk of genetic diseases. 77.2% increase in situs abnormality for PCD patients with consanguineous parents compared with non-consanguineous parents (Best et al., 2019). In a highly consanguineous British Asian population, a high prevalence of PCD was reported at 1 in 2265(O'Callaghan et al., 2010). According to a cross-sectional study carried out in Saudi Arabia studied the characteristics of PCD patients in

this area, 93% of the study participants had a history of parental consanguineous (Asseri et al., 2023).

Regarding the prevalence of clinical manifestations of the participants, 85% reported nasal congestion, 50% reported hearing problems and chest pain, and approximately 37% complained of headache. 90% of respondents reported having a productive cough with 75% viscous sputum consistency. Consistent with our findings, other studies have reported similar symptoms and clinical features. A systematic review and meta-analysis (Goutaki et al., 2016) studied the clinical manifestation of PCD patients. According to the study's findings, situs anomalies were reported in 49% of the weighted mean of the studies. Regarding the symptoms of the upper respiratory tract, 75% of weighted mean studies reported nasal congestion or rhinitis, 74% reported otitis media, and 69% sinusitis. In terms of symptoms related to the lower respiratory tract, cough was reported at 88% of the weighted mean of the studies, 89% was characterized by sputum production, and a prevalence of bronchiectasis was reported at 56% of the weighted mean of the studies (Goutaki et al., 2016). In another study conducted in Switzerland (Goutaki et al., 2022), respiratory symptoms were evaluated in 74 patients with PCD. Of these, 94% reported chronic nasal symptoms, 58% reported ear pain and hearing issues, and nearly all 99% reported coughing and sputum production.

Respiratory tract bacterial infections are common in PCD (Piatti et al., 2020), studies that aimed to determine the prevalence of the most common respiratory pathogens in PCD patients, reported that Haemophilus influenzae was the most common pathogen followed by Staphylococcus aureus. Additional bacterial species commonly recovered from sputum samples of patients with PCD include Staphylococcus aureus, Pseudomonas aeruginosa, and Streptococcus pneumoniae (Roden et al., 2019; Wijers et al., 2017). Correspondingly, in our study population, Haemophilus influenzae was the most common followed by Staphylococcus aureus.

Regarding sex, the present study found no statistically significant differences in lung function between the sex groups. Halbeisen et al found that males had higher FEV_1 than females (Halbeisen et al., 2018). The reason for this difference was not well known, it was suggested that progesterone is associated with an inhibition of the mucociliary transport function, which may be a factor in the sex difference (Jain et al., 2012). On the other hand, other studies did not

show evidence of an association between lung function and sex (Halbeisen et al., 2021; Shah et al., 2016).

Between the two age groups (6–12 years and 13–18 years), our results showed no statistically significant differences in lung function. Similar findings were found in a cross-sectional study stratified analysis by age group (children under 18 and adults over 18), FEV_1 did not decline with age (Boon et al., 2014). In contrast, age-related reductions in FEV_1, FVC, and FEV_1/FVC were found in a study evaluating lung function in PCD patients from school age to adulthood, not all patients experienced these reductions at the same rate. In 21% of patients, FEV_1 increased over time; in 40%, it stayed stable; and in 39%, it decreased (Halbeisen et al., 2021). Furthermore, a systematic review and meta-analysis examined the spirometric incidence of PCD patients and concluded that FEV_1 and FVC were lower in adults >18 years than in children <18 years (Halbeisen et al., 2019).

Concerning functional exercise capacity, our findings revealed no statistically significant differences in walking distance between sex groups and between age groups. Likewise, a compared study between children and young adults with PCD to healthy controls showed reduced aerobic fitness. Neither gender nor age was linked to this decrease (Madsen et al., 2013b).

Considering the PCD QOL questionnaire, our study observed no statistically significant difference between the sex groups. A systematic review (Behan et al., 2017b) found that, in PCD patients, health-related quality of life declines with age, regardless of gender.

The current study evaluated the impact of ACBT and OPEP therapy on lung function parameters using the following measures: FEV_1, FVC, FEV_1/FVC, and the $MEF_{25-75\%}$. In our findings, FEV_1 showed that there was a statistically significant difference ($p<0.05$) in favor of using the OPEP Cohen's d= 0.86. Similar to our finding, a comparative study found that employing OPEP with lower respiratory tract infections improved lung function by improving oxygenation, reducing inflammation, and improving sputum drainage compared with the mechanical percussion technique (Ni et al., 2018).

In terms of FVC and FEV_1/ FVC parameters, our results showed that there was no statistical significance in both groups $p>0.05$. The findings are consistent with similar studies, a

randomized crossover trial compared ACBT versus Acapella in bronchiectasis (Patterson et al., 2005), and another randomized crossover trial compared ACBT versus Flutter in no cystic fibrosis bronchiectasis (Üzmezoğlu et al., 2018b), concluded that ACBT and OPEP have similar effects on lung function parameters. Furthermore, a systematic review that studied the effects of OPEP therapy in adults with non-cystic stable bronchiectasis, showed a similar effect of OPEP with other ACTs on lung function (A. L. Lee et al., 2015b).

According to $MEF_{25-75\%}$ of our data, there was a statistically significant difference ($p<0.05$) between the two groups, the mean of the OPEP was higher, Cohen's d= 0.76. This finding may be explained that $MEF_{25-75\%}$ is the most sensitive measure of airflow in medium to small airways. A decrease in this number signifies an impairment of these peripheral airways (Kwon et al., 2020). As the positive expiratory pressure mechanism in OPEP devices, the exhalation through the device decreases airway collapsibility and facilitates collateral ventilation, making it easier for secretions to move centrally (Alghamdi et al., 2020). An interesting study focused on the effectiveness of improving small airway resistance in COPD using the Aerobika device, the results showed that there was a statistically significant improvement in FEV_1 and $MEF_{25-75\%}$ after 12 and 24 weeks of a single-arm intervention study (Sahardin et al., 2023b).

Field walking tests are widely used to assess exercise capacity, which is a crucial indicator of respiratory-related function. 6MWT is a valid and reliable field walking test (Holland et al., 2014b). In our study, exercise functional capacity using the 6-minute walk test revealed statistically significant results favoring OPEP ($p< 0.05$), with an effect size indicated by Cohen's d of 0.71. Our findings align with the results of (Murray et al., 2009) who found that after the use of Acapella twice daily for three months with non-cystic fibrosis bronchiectasis patients, the incremental shuttle walk test distance improved. Also, in a prospective randomized controlled trial study for CF patients, a modified shuttle test was used to evaluate exercise tolerance for five different ACT techniques including ACBT, AD, PEP, and OPEP. There were no statistically significant differences between the five treatment groups at the end of the study ($P = 0.52$) (Pryor et al., 2010).

A quality-of-life assessment is essential for people with chronic diseases that are considered long-term health conditions that affect an individual's quality of life in different areas. In addition to assisting with medical management, it directs personalized care and encourages

communication between patients and healthcare providers (Megari, 2013). Due to this, the researcher in this study needed to develop a specific Arabic questionnaire for PCD patients, whose ages ranged from 6 to 18.

In our study, there was no statistical significance found in the results obtained after re-completing the questionnaire. The QOL total score in both groups was positively impacted, even though there was no statistical significance. Our results are consistent with prior research indicating that using the flutter device or ACBT in non-CF bronchiectasis showed no significant change using the Chronic Respiratory Disease Questionnaire during the intervention (Thompson et al., 2002). Another prospective randomized comparative study between Flutter and ACBT in patients with bronchiectasis showed no statistical difference in sub-scores of the Short Form – 36 Quality of Life Questionnaire (Üzmezoğlu et al., 2018a).

Concerning the correlations analyzed between the main variables, the study showed a strong positive correlation between FEV_1 and FVC lung function parameters p= 0.00. A moderate correlation between age, FEV_1, FVC, and distance walked in the 6-minute walk test p= 0.00 for either FEV_1 and FVC and a weak positive correlation between the PCD QOl questionnaire and the walking distance p= 0.03. According to a study that evaluated physical activity and sedentary behavior in adult CF patients, there was a positive statistically significant correlation between physical activity and lung function, quality of life, sleep, and aerobic capacity (Curran et al., 2022). Madsen et al studied aerobic fitness in children and young adults with PCD, one of the findings was that there was a positive correlation between FEV_1 and aerobic fitness. (Madsen et al., 2013b).

Just to highlight, and based on participant feedback, the device's use has been beneficial because it is portable, simple to use, and aids in sputum clearance. A systematic review examined the effect of ACT on bronchiectasis. In two studies, participants preferred OPEP devices over the ACBT or postural drainage techniques (Phillips et al., 2020).

4.3 Study limitations

The researcher noted that the current study had some limitations and suggested that they may be taken into consideration in future research:

- The study's inclusion criteria were limited to stable PCD patients and didn't evaluate those in acute exacerbation.
- A longer duration follow-up might be required to evaluate the long-term efficacy of the intervention in PCD patients.
- As the required intervention was based on a home-based treatment, there was a possibility of compliance and adherence issues. There was still a chance that participants would not adhere, even though we offered a mid-term follow-up, motivational calendars, and regular phone calls to encourage adherence.
- Because of the unstable political situation, several participants refused to take part in the study.

Strengths of the current study:

- This is the first study in Palestine that studies the effectiveness of two different ACTs in PCD patients.
- It is important to highlight that PCD disease, even if it is worldwide is considered a rare disease. The number of consanguineous marriages in Palestine and the Arab world is relatively high. Moreover, based on my professional experience, healthcare providers and medical professionals are not well-versed in this illness.
- In Palestine, the use of OPEP devices for chronic lung diseases is uncommon. The Aerobika device was a step toward raising awareness of the value of a range of ACTs.
- The pre-, mid-, and post-tests were conducted by a blinded assessor to prevent assessors' bias.

5. Chapter five

Conclusion and recommendations

5.1 Conclusion

5.2 Recommendations

5.1 Conclusion

In this study, the effects of ACBT and OPEP on exercise functional capacity, lung function, and the PCD QOL questionnaire in children with PCD were investigated using a randomized comparison trial design. Thirty-two children from the West Bank- Palestine participated in the study and were assigned randomly to either group. Pre-, mid-, and post-tests were conducted at Caritas Baby Hospital- Bethlehem as a follow-up to the three-month home-based program that served this interventional study.

Based on our results, the researcher concluded the following:

- The findings of this study support the evidence that PCD is a rare inherited autosomal recessive disease, where 87.5% of participants reported a positive history of parental consanguinity.
- The main clinical manifestations of the participants were nasal congestion, hearing problems, and chest pain. Cough was characterized as productive with a viscous consistency. Haemophilus influenzae is considered the most common respiratory pathogen followed by Staphylococcus aureus.
- In terms of lung function outcome, a statistical significance difference of FEV_1 ($p= 0.02$) and $MEF_{25-75\%}$ ($p= 0.03$), OPEP was more effective than ACBT with an effect size (Cohen's $d=0.86$) for the FEV_1 and (Cohen's $d=0.76$) for $MEF_{25-75\%}$. On the other hand, there was no statistical significance for the FVC and FEV_1/FVC.
- The functional exercise capacity measured by the 6-minute walk test, showed a statistical significance of the walked distance ($p=0.05$), in favor of the OPEP group with greater walking distance with an effect size (Cohen's $d=0.71$).
- Regarding the PCD QOL questionnaire, both ACBT and OPEP demonstrated a positive influence on the overall QOL score; there was no statistically significant difference between the two groups.
- There was a strong positive statistical correlation between FEV_1 and FVC, and a moderate positive correlation between age, FEV_1, FVC, and distance walked in the 6-minute walk test. Additionally, a weak positive correlation was found between the PCD QOL questionnaire and the walking distance.

5.2 Recommendations

Recommendations for healthcare providers:

- It is essential to increase the knowledge among clinicians about PCD, the importance of early diagnosis, evidence-based care, and multidisciplinary management is crucial.
- Increase awareness of physiotherapists and health care providers the importance of airway clearance techniques which is a cornerstone in the management of chronic lung diseases such as PCD.
- The physiotherapist needs to educate PCD patients on proper daily breathing techniques, the importance of maintaining an active and healthy lifestyle, and strategies for managing their respiratory conditions at home.
- Healthcare providers must raise awareness about the potential risks associated with parental consanguinity.

Recommendations for the researchers:

- Further research is required to develop a clinical practice guideline to optimize physiotherapy management in PCD.
- It is recommended that future studies examine the impact of different ACTs for long-term effects.
- To build upon the current findings, future research with a larger sample size is needed.

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Appendixes:

Appendix 1: Data collection sheet

Appendix 2: American Thoracic Society (ATS) Statement: Guidelines for the Six-Minute Walk Test

Appendix 3: Quality of life questionnaire for patients with Primary Ciliary Dyskinesia (From 6- 18 years old)

Appendix 4: A monthly calendar

Appendix 5: Ethical approval of Al-Quds University Research Ethical Committee

Appendix 6: Ethical approval of Caritas Baby Hospital Medical Research Committee

Appendix 7: Informed consent

Appendix 1: Data collection sheet

جمع بيانات مرض خلل حركة الأهداب الأولية

تاريخ التقييم: _____

1. البيانات الديموغرافية:
   1) رقم المريض: _____
   2) الجنس:
      1- ذكر
      2- أنثى
   3) العمر: _____
   4) مكان السكن:
      1- بيت لحم
      2- القدس
      3- الخليل
      4- رام الله
      5- مكان اخر

      _____

2. التاريخ العائلي:

   1) درجة قرابة الوالدين:
      1- توجد قرابة
      2- لا توجد قرابة

   2) أشقاء آخرون مصابون بخلل حركة الأهداب الأولية
      1- نعم
      2- لا
      3- اذا كانت الاجابة نعم، كم عددهم؟

      _____

3. هل تم الحصول على أية أدوية سواء كانت عن طريق الفم أو الوريد في آخر 3 أشهر:
   1- لم يتم الحصول على أية أدوية

2- مضادات حيوية
3- اذا كانت الاجابة 2، كم عدد الدورة العلاجية؟

_____

4. آخر زراعة بلغم (خلال اخر شهر):
   1- Haemophilus influenzae
   2- Pseudomonas aeruginosa
   3- Staphylococcus aureus
   4- Streptococcus pneumonia
   5- أخرى

_____

5. خصائص السعال:
   1- منتج للبلغم
   2- جاف
   3- صفير
   4- أخرى

_____

6. صفات البلغم:
   1- سلس
   2- سميك
   3- لزج
   4- أخرى

_____

7. لون البلغم:
   1- شفاف
   2- أصفر
   3- أخضر
   4- بني
   5- مصحوب بالدم

8. الأعراض المصاحبة

		نعم	لا
1	وجع في الرأس		
2	مشاكل في السمع		
3	إحتقان أنفي		
4	تغييرات في الصوت		
5	حرارة		
6	وجع في الصدر		
7	تعجر أو تقوس الأصابع		
8	أعراض أخرى		

Appendix 2: American Thoracic Society (ATS) Statement: Guidelines for the Six-Minute Walk Test

APPENDIX

The following elements should be present on the 6MWT worksheet and report:

Lap counter: _____ _____ _____

Patient name: _____ Patient ID# _____

Walk # _____ Tech ID: _____ Date: _____

Gender: M F Age: ____ Race: ____ Height: ___ft ____in, ____ meters

Weight: _____ lbs, _____kg Blood pressure: _____ / _____

Medications taken before the test (dose and time): _____

Supplemental oxygen during the test: No Yes, flow _____ L/min, type _____

	Baseline	End of Test
Time	___:___	___:___
Heart Rate	_____	_____
Dyspnea	____	____ (Borg scale)
Fatigue	____	____ (Borg scale)
SpO_2	____ %	____%

Stopped or paused before 6 minutes? No Yes, reason: _____

Other symptoms at end of exercise: angina dizziness hip, leg, or calf pain

Number of laps: ____ (×60 meters) + final partial lap: _____ meters =

Total distance walked in 6 minutes: _____ meters

Predicted distance: _____ meters Percent predicted: _____%

Tech comments:

Interpretation (including comparison with a preintervention 6MWD):

Appendix 3: Quality of life questionnaire for patients with Primary Ciliary Dyskinesia (From 6- 18 years old)

استبيان جودة الحياة لمرضى خلل حركة الأهداب الأولية

الفئة المستهدفة (6- 18 عام)

صمم هذا الاستبيان بهدف التعرف على مدى تأثير مرض خلل حركة الأهداب الأولية الذي يسببه في الحياة والنشاطات اليومية والتأثير على الفعاليات الاجتماعية والمدرسية. كما سيساعد الفريق الطبي من استخدام اجاباتك ودرجة الاستبيان التي حصلت عليها من أجل تحسين معالجة مرضك والحصول على الاستفادة القصوى من العلاج.

الرجاء قراءة كل فقرة ووضع علامة في المربع الذي يتناسب مع أفضل خيار فيما يتعلق في الحالة الصحية لديك/ي خلال الاسبوع الماضي. يرجى الاجابة على جميع الأسئلة مع التأكد من اختيار اجابة واحدة فقط.

ملاحظة: يمكن للأهل مساعدة الطفل في الإجابة عن الاستبيان عند الحاجة.

رقم الشخص: _____

التاريخ: _____

رقم سؤال	النشاطات اليومية والجسدية خلال الاسبوع الماضي	أبداً	بعض الأحيان	دائماً
-1	ما مدى تأثير السعال على حياتك اليومية؟			
-2	ما مدى انزعاجك من السعال يومياً؟			
-3	ما مدى سهولة شعورك بالارهاق من السعال؟			
-4	ما مدى تأثر نومك بمشاكلك التنفسية؟			

5-	ما مدى تأثير مشاكلك التنفسية على نشاطاتك اليومية في المنزل، مثل ارتداء الملابس والاغتسال؟			
	ما مدى تأثير مشاكلك التنفسية عند عمل نشاطات جسدية متوسطة، مثل:	أبداً	بعض الأحيان	دائماً
6-	المشي			
7-	صعود الدرج			
8-	حمل الاشياء			

	ما مدى تأثير مشاكلك التنفسية عند القيام بالنشاطات الجسدية المرهقة، مثال:	أبداً	بعض الأحيان	دائماً
9-	الركض			
10-	ممارسة الرياضة			

رقم سؤال	الفعاليات الاجتماعية والمدرسية خلال الاسبوع الماضي	أبداً	بعض الأحيان	دائماً
	ما مدى تأثير مشاكلك التنفسية عند القيام بالنشاطات الاجتماعية، مثال:			
11-	التكلم			

12-	اللعب مع الاطفال أو الحيوانات الأليفة			
13-	زيارة الأصدقاء والأقارب			
14-	ما مدى تأثير مشاكلك التنفسية على حضورك المدرسيّ			
15-	ما مدى تأثير مشاكلك التنفسية على آدائك المدرسيّ			

الاستبيان مكون من 15 سؤال كما هو مبين في الجدول:

رقم السؤال	الأنشطة	النتيجة
1 - 5	النشاطات اليومية	
6- 10	النشاطات الجسدية	
11 - 15	الفعاليات الاجتماعية والمدرسية	

تم اعتماد مقياس ليكرت الثلاثي في هذا الاستبيان للاجابة على الأسئلة كما مبين أدناه:

الاجابة	النتيجة
أبداً	3
بعض الأحيان	2
دائماً	1

مؤشر النتيجة الإجمالية:

النتيجة الإجمالية	المعيار
45 - 39	ممتاز
38 - 33	جيد جداً
32 - 27	جيد
26 - 21	مقبول
20 - 15	سيء

Appendix 4: A monthly calendar

	الاثنين	الثلاثاء	الاربعاء	الخميس	الجمعة	السبت	الاحد
فتره الصباح							
	☆	☆	☆	☆	☆	☆	☆
	☆	☆	☆	☆	☆	☆	☆
فتره الظهر							
	☆	☆	☆	☆	☆	☆	☆
	☆	☆	☆	☆	☆	☆	☆

ملاحظات:

	الاثنين	الثلاثاء	الاربعاء	الخميس	الجمعة	السبت	الاحد
فتره الصباح							
	☆						
	☆						
فتره الظهر							
	☆						
	☆						

ملاحظات:

Appendix 5: Ethical approval of Al-Quds University Research Ethical Committee

Al-Quds University
Jerusalem
Deanship of Scientific Research

بسم الله الرحمن الرحيم

جامعة القدس
القدس
عمادة البحث العلمي

Research Ethics Committee
Committee's Decision Letter

Date: Jun 11th, 2022
Ref No: 237/REC/2022

Dears Dr. Hadeel Halaweh, Ms. Bishara Fashho,

Thank you for submitting your application for research ethics approval. After reviewing your application entitled "A randomized comparative study of active cycle breathing technique versus positive expiratory pressure therapy on lung function and quality of life in children with primary ciliary dyskinesia" the Research Ethics Committee confirms that your application is in accordance with the research ethics guidelines at Al-Quds University.
We would appreciate receiving a copy of your final research report/ publication.

Thank you again and wish you a productive research that serves the best interests of your subjects.

PS: This letter will be valid for two years.

Sincerely,

Suheir Ereqat, PhD
Associate Professor of Molecular Biology

Research Ethics Committee Chair

Cc. Prof. Imad Abu Kishek - President
Cc. Members of the committee
Cc. file

Abu-Dies, Jerusalem P.O.Box 20002
Tel-Fax: #970-02-2791293
research@admin.alquds.edu
ابوديس، القدس ص.ب. 20002
تلفاكس: #970-02-2791293

Appendix 6: Ethical approval of Caritas Baby Hospital Medical Research Committee

Children's Relief **Bethlehem**

Caritas Baby Hospital
P.O.Box 84, Bethlehem
Tel. +972 2 275 85 00, Fax +972 2 275 85 01
info@crb-mail.org, www.childrens-relief-bethlehem.org
Arab Bank, Bethlehem, Acct. 702200

Medical Research Agreement of Principles

Date: 15-10-2022

This is to certify that Caritas Baby Hospital represented by: __**Asma Siman and Dr. Nisreen Rumman**___will be collaborating with ____ **Alquds University** _____ represented by: _ **Dr. Hadeel Halaweh** ___ to conduct a Medical Research Project entitled: _ A randomized comparative study of active cycle breathing technique versus oscillating positive expiratory pressure therapy on lung function and quality of life in children with primary ciliary dyskinesia ___. The research project will be conducted by: _____**Bishara Fashho** _____.

The above research project was reviewed by members of the Caritas Medical Research Committee and was approved on____**15-10-2022**_____ and given MRC-Project Number _____**MRC-46**_____.

After the fruitful accomplishment of the project both parties agree to publish the work in peer peer-reviewed journal and the authorship location in the manuscript will be as follows:

First author: **Bishara Fashho**
Second author: Dr. Hadeel Halaweh
Third author:
Before last author:
Last author: **Dr. Nisreen Rumman**

Principle Investigator

Asma Siman &
Dr. Nisreen Rumman

Caritas Baby Hospital
Medical Research Committee Representative

Dr. Musa Hindiyeh

Appendix 7: Informed consent

A randomized comparative study of active cycle of breathing technique versus oscillating positive expiratory pressure therapy on lung function and quality of life in children with primary ciliary dyskinesia

دراسة مقارنة عشوائية بين تقنية الدورة النشطة للتنفس والعلاج بواسطة ضغط الزفير الإيجابي المتذبذب على وظائف الرئة وجودة الحياة عند الأطفال الذين يعانون من خلل حركة الأهداب الأولية

اسم الباحث

بشارة حنا فشحو

إشراف

الدكتورة: هديل حلاوة

نموذج تعريف بالبحث

<u>عنوان البحث:</u> دراسة مقارنة عشوائية بين تقنية الدورة النشطة للتنفس والعلاج بواسطة جهاز ضغط الزفير الإيجابي المتذبذب على وظائف الرئة وجودة الحياة عند الأطفال الذين يعانون من خلل حركة الأهداب الأولية

نشكر لكم استعدادكم للمشاركة بهذا البحث الذي هو جزء من دراسة الماجستير في العلاج الطبيعي/ جامعة القدس. هذا البحث يهدف الى تقييم فاعلية الأساليب العلاجية المستخدمة في وظائف الرئة وجودة الحياة عند الأطفال. من خلال:

تطبيق أدوات التقييم التي سوف تستخدم في هذا البحث وهي أدوات قياس آمنه ولا يوجد منها اي ضرر على الطفل، حيث تتضمن فحص وظائف الرئة، فحص المشي لمدة 6 دقائق واستبيان جودة الحياة لمرضى خلل حركة الأهداب الأولية.

سيكون هناك فحوصات قبلية في بداية البحث، فحوصات في وسط فترة البحث وفحوصات بعد 3 أشهر من تطبيق البرنامج العلاجي

سيقوم الباحث بإجراء البحث بالتعاون مع أهل الطفل والمعالج/ة الفيزيائي/ة.

ان اشتراككم في هذا البحث هو طوعي ومرتبط بتوقيعكم على نموذج موافقة بالمشاركة وتصريح بفهمكم لطبيعة البحث وأهدافه، وأدوات القياس المستخدمة فيه. وفي حال وجود أي استفسار عن البحث او أي شيء متعلق بهذه الدراسة، يرجى التواصل مباشرة مع الباحث (بشارة حنا فشحو)على الرقم التالي 0598454954

شاكرين لكم حسن تعاونكم

أ. بشارة حنا فشحو

بكاوريوس علاج طبيعي

طالب ماجستير علاج طبيعي

جامعة القدس

نموذج الموافقة على المشاركة في البحث

Code NO

عزيزي الوالد /الوالدة

توقيعك ادناه على نموذج الموافقة هذا هو بموجب موافقة مكتوبة وموقعة على مشاركة طفلك/ طفلتك في دراسة بحثية سيقوم بها الباحث بشارة حنا فشحو بعنوان " دراسة مقارنة عشوائية بين تقنية الدورة النشطة للتنفس والعلاج بواسطة ضغط الزفير الإيجابي المتذبذب على وظائف الرئة وجودة الحياة عند الأطفال الذين يعانون من خلل حركة الأهداب الأولية". وهو اقرار بأنه قد تم شرح أهداف البحث وطرق الفحص وتطبيق أدوت القياس للبحث وإنه قد تم شرح الحقوق المتضمنة:

سرية المعلومات التي تصرح بها وعدم اطلاع اي شخص عليها وتخزينها في مكان آمن لا يصل اليه سوى الباحث.

استخدام المعلومات للأغراض العلمية فقط

حرية انسحابك في اي وقت من الدراسة ومن دون الحاجة لإبداء الاسباب ودون اية عواقب.

حقك في الاطلاع على نتيجة الفحوصات ونتائج البحث النهائية

موافقة المشارك

لقد تم وصف الدراسة البحثية لي شفهيا، وبما فيه المعلومات المدرجة أعلاه، واوافق على المشاركة بهذه الدراسة البحثية.

اسم الطفل الرباعي: _____

اسم والد أو والدة الطفل: _____

توقيع الوالد أو الوالدة:_____

التاريخ: _____