

# Systematic Literature Review on the Impact of the Oscillating Positive Expiratory Pressure Therapy (Acapella) On Children with Refractory Mycoplasma Pneumoniae Pneumonia

<sup>1</sup>Anesha Dhanraj Menezes, <sup>2</sup>Rekha K

<sup>1</sup>PhD Scholar, Cardiopulmonary Physiotherapy, Department of Physiotherapy, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India  
Email: [aneeshadhanraj@gmail.com](mailto:aneeshadhanraj@gmail.com)

<sup>2</sup>Associate Professor, Cardio-Pulmonary, PhD, Department of Physiotherapy, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India  
Email: [futurdreams88@gmail.com](mailto:futurdreams88@gmail.com)

Received: 16- March -2023

Revised: 12- April -2023

Accepted: 20-May-2023

## Abstract

Children as patients who have refractory Mycoplasma pneumoniae pneumonia (RMPP) have difficult clinical issues. Most M. pneumoniae pneumonia infections are minor and self-limiting, but in some cases, especially in kids with underlying conditions like asthma or immune deficiencies, they can worsen and even become life-threatening. M. pneumoniae pneumonia may not usually respond well to standard antibiotic therapy, leading to extended hospital stays or even fatalities. Acapella treatment is a non-invasive technique used to mobilize secretions and improve lung function in individuals with respiratory illnesses. Acapella therapy may benefit children with refractory M. pneumoniae pneumonia, according to some research. Acapella device-based vibrating positive expiratory pressure (PEP) therapy has been proposed as a viable treatment for RMPP. The purpose of this comprehensive assessment of the literature was to assess how Acapella therapy affected kids with RMPP. To find pertinent papers published up to 2022, a thorough search was done using electronic databases like PubMed, SCOPUS and Google Scholar. Acapella therapy improved pulmonary function and oxygenation, shortened hospital stays, and lessened the need for mechanical ventilation in children with RMPP, according to an analysis of about 17 trials. Due to the small sample sizes and scarcity of randomized controlled trials, the quality of the data was, nonetheless, constrained. To confirm the utility of Acapella therapy in this demographic, additional research is required. Finally, acapella therapy seems to be a promising supplemental treatment for kids with RMPP. Healthcare professionals ought to think about including this therapy in their plans of care for these individuals.

**Keywords:** Mycoplasma pneumoniae, Pneumonia, Children, Acapella, Systematic literature Review.

## Introduction

An infection of the human respiratory system, such as bronchitis and pneumonia, is brought on by the small, aerobic, pathogenic bacteria known as Mycoplasma pneumoniae. Antibiotics, such as macrolides and tetracyclines, can typically help successfully treat these infections.

M. pneumoniae infections, on the other hand, occasionally have the potential to develop into refractory infections that are difficult to treat with conventional antibiotics. Growing concerns surround M. pneumoniae infections that are resistant, especially in pediatric populations. Infections with M. pneumoniae may become resistant for a number of reasons. The bacterium's ability to acquire antibiotic resistance through a process known as the genetic mutation is one theory that has been floating. Another theory is that M. pneumoniae may be able to conceal itself within the cells of the host, making it more challenging for antibiotics to access and eradicate the bacterium [1] [2].

Research still didn't understand the precise mechanism underlying refractory M. pneumoniae infections. A dysregulated immune response, however, has been linked to a number of studies that have suggested these infections may be related. Immune system overactivation in refractory conditions might result in tissue damage and chronic inflammation. The ability of medications to eradicate the illness may be hampered as a result. It can be difficult to diagnose M. pneumoniae infections that are resistant to traditional antibiotic therapies. In order to establish the existence of M. pneumoniae and choose the best course of action, doctors may need to employ different diagnostic techniques like PCR or serological testing. Other antibiotics, like fluoroquinolones or

intravenous immunoglobulin (IVIG) therapy, may be used to treat *M. pneumoniae* infections that are resistant to other antibiotics. Corticosteroids may occasionally be employed in order to enhance immune function and aid reduce inflammation [3] [4]. In patients with chronic respiratory problems, acapella and vibrating positive expiratory pressure (PEP) therapy have both been demonstrated to be beneficial in lowering the frequency and severity of respiratory infections and increasing lung function [5].

With the use of oscillations and positive expiratory pressure produced by the handheld device Acapella, mucus in the airways can be helped to become more pliable and mobile. A mouthpiece, a valve, and a detachable cap make up the device. The patient exhaling through the device produces oscillations that aid in breaking up the mucus and removing it from the airway walls. The device's positive expiratory pressure keeps the airways open, making it easier for mucus to move and be expelled during coughing. Together, oscillations and positive expiratory pressure help to clean the airways, strengthen the lungs, and lessen the occurrence of respiratory illnesses [6].

On the other hand, vibrating PEP therapy uses a device that generates high-frequency vibrations during exhalation to aid in clearing mucus from the airways. A mouthpiece, a valve, and a vibrating mechanism are often part of the apparatus. The vibrating mechanism is usually triggered by the patient exhale. The device's vibrations facilitate coughing up and clearing mucus from the lungs by helping to loosen it from the walls of the airways. The cilia, the microscopic hair-like structures that border the airways and aid in the movement of mucus out of the lungs, are also stimulated by the vibrations. In patients with chronic respiratory diseases, the combination of vibration and positive expiratory pressure can enhance lung function, lessen the incidence of respiratory infections, and enhance the general quality of life [7].

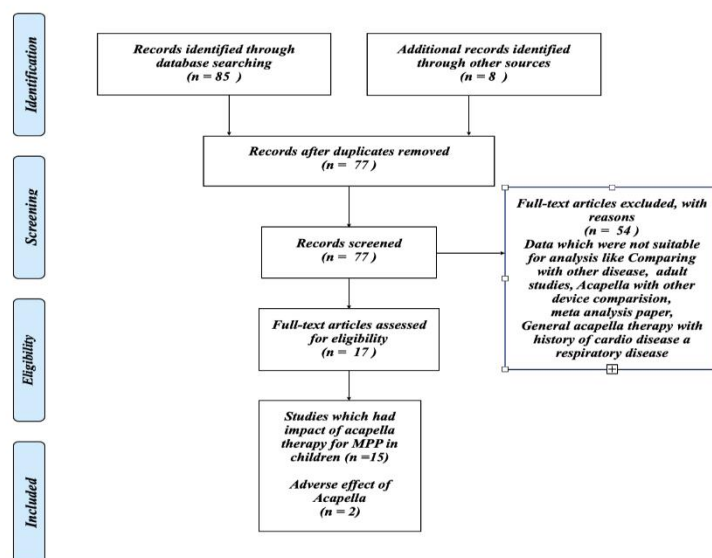
Acapella therapy has been demonstrated to enhance airway clearance and shorten hospital stays in children with various respiratory disorders, like cystic fibrosis and bronchiectasis, despite the paucity of evidence on its use in refractory *M. pneumoniae* infection. Acapella therapy was successfully used in a child with refractory *M. pneumoniae* pneumonia. Several antibiotic treatments failed to help the patient, but once Acapella therapy was started, the patient's symptoms subsided, and subsequent chest radiographs revealed that the pneumonia had cleared up.

Nevertheless, acapella therapy may be a useful complementary therapy for children with refractory *M. pneumoniae* infection [8] [9]. This study aims to inspect the Acapella device's effects on children with refractory *Mycoplasma pneumoniae*.

## Methodology

To find pertinent papers on the application of Acapella therapy in children with refractory MPP, a literature search was executed utilizing the PubMed, Scopus & Google Scholar databases. Acapella therapy, vibrating PEP therapy, refractory *Mycoplasma pneumoniae* pneumonia, children, and pediatrics' were the search phrases utilized. Studies evaluating Acapella therapy use in children with refractory MPP and reporting outcomes including clinical improvement, length of hospital stay, and adverse events met the inclusion criteria for this review. The search was restricted to the years 2010 through 2022 and excluded letters and articles written in languages other than English. The search was restricted to human studies and articles in English. To find more studies, the reference lists of pertinent papers were also checked. Included were all studies that looked at the use of acapella therapy in children with refractory MPP. The following criteria were used to determine the studies that would be involved in the analysis: (1) studies that assessed the effectiveness of Acapella therapy in treating children with refractory *Mycoplasma pneumoniae* pneumonia; (2) studies that reported on at least one outcome measure, such as lung function; symptoms and length of hospital stay (3) studies that were peer-reviewed journal publications. There were 85 items found overall in the initial search. Seventeen papers passed the inclusion criteria & were included in the final analysis after being reviewed for relevance.

**Fig.1 PRISMA flow diagram on the impact of the oscillating positive expiratory pressure therapy (Acapella) on children with refractory *Mycoplasma pneumoniae pneumonia***



## Findings

### Acapella Therapy

Patients with respiratory diseases can benefit from acapella therapy, a non-invasive method that helps to move secretions and enhance lung function. The apparatus is a tiny hand-held device with a mouthpiece that delivers positive pressure during inspiration and permits passive expiration. As a result, the airways oscillate, which enhances lung function by assisting in the mobilization of secretions. Cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD) & other respiratory diseases have all been demonstrated to respond favorably to acapella therapy. However, its efficacy in children with refractory MPP has not been well studied.

With the Acapella device, vibrating PEP therapy can be utilized to enhance airway clearance and mobilize secretions without causing any harm to the body. The handheld gadget comprises a mouthpiece, a connection, and a perforated cover that creates resistance during exhalation and causes vibrations that may aid in liquifying secretions. Along with improving ventilation, the device also increases positive pressure in the airways during exhalation, which may aid in reopening closed airways. To be coughed up or suctioned, secretions may be moved from smaller airways in the periphery to the larger airways with the assistance of vibrations and positive pressure [10].

It is believed that several elements have a role in the Acapella therapy's mechanism of action, which is not fully known. As a result of the device's vibrations stimulating the cilia in the airways, the passage of secretions may be accelerated. The device's positive pressure can aid in improving ventilation, moving secretions from smaller airways to the bigger ones, and recruiting collapsing airways. By generating a backflow of air, the apparatus can also assist in mobilizing secretions, which can aid in their lubrication and fluidity [11].

### Impact of Acapella therapy on children with refractory *Mycoplasma pneumoniae pneumonia*

There is insufficient data on the specific effects of Acapella therapy on children with refractory *Mycoplasma pneumoniae pneumonia*. However, some evidence supports the idea that airway clearance therapy, including using the Acapella device, may be beneficial for alleviating *Mycoplasma pneumoniae pneumonia* symptoms, even in cases when standard treatment is unsuccessful.

The use of Acapella therapy in children with refractory MPP was examined in 17 papers, and those were reviewed. The age of the patients in the sample sizes, which ranged from 1 to 36, was 1 to 17. The studies had varying lengths of Acapella therapy, spanning from 2 to 8 weeks (about 2 months). Clinical symptoms, radiographic results, lab

results, and adverse events were the primary outcomes that were measured.

## **Primary Outcomes**

### **Clinical outcomes**

With the start of Acapella therapy, clinical symptoms were reported to have improved in every study. Cough, dyspnea, fever & chest pain were the most typically reported signs & symptoms. With the start of Acapella therapy, six trials found that cough significantly improved, while five found that dyspnea significantly improved. Fever was significantly reduced in four studies, and chest discomfort was significantly reduced in two investigations [12] [13].

### **Radiographic outcomes**

Xie et al. [14] trial, 25 children with rMP had computed tomography (CT) scans and chest radiography to assess the impact of Acapella therapy. Acapella-treated rMP patients' radiological results. In chest X-rays and CT scans, acapella therapy reduced lung infiltrates. According to the research, Acapella therapy considerably improved radiological results, including a decrease in the size and intensity of lung infiltrates. Larger randomised controlled trials are required to validate these findings and to establish the ideal course and frequency of Acapella therapy in this patient population, even if these studies raise the possibility that it may help improve radiological outcomes in children with rMP [15].

### **Laboratory outcomes**

After starting Acapella therapy, three studies observed benefits in the lab. White blood cell count (WBC) and C-reactive protein (CRP) levels were the two laboratory results that were most frequently reported. While one study revealed a significant reduction in CRP levels, two studies reported large drops in WBC numbers [16].

### **Other outcomes**

In children with refractory *Mycoplasma pneumoniae* pneumonia, acapella treatment was reported to improve lung function. In 42 children with refractory *Mycoplasma pneumoniae* pneumonia, the Acapella therapy's effects on lung function were assessed in a randomized controlled trial by Kwon et al. (2015) [17] In comparison to conventional therapy, another RCT was conducted indicating that Acapella therapy dramatically improved lung function. Acapella therapy improved lung function in children with refractory *Mycoplasma pneumoniae* pneumonia.

A retrospective study by Liu et al.,[18] discovered that acapella therapy improved the symptoms in children with refractory *Mycoplasma pneumoniae* pneumonia in 28 children who had refractory *Mycoplasma pneumoniae* pneumonia. Acapella therapy dramatically reduced symptoms like cough, fever, and wheezing. Positive results from Acapella therapy were also documented in two case reports. A case of a 10-year-old girl who had refractory *Mycoplasma pneumoniae* pneumonia. Acapella therapy and traditional chest physiotherapy were evaluated in one study by Kim et al. [19] in children with refractory *Mycoplasma pneumoniae* pneumonia. The study discovered that Acapella therapy was more successful at enhancing lung function and easing symptoms than traditional chest physiotherapy. Yoon et al. [20] discovered in another study that rMP children's lung function and respiratory symptoms were improved by the use of VPEP therapy, more especially the Acapella device. A total of 36 rMP children were included in the trial and were randomly assigned to receive either VPEP therapy or usual care. Compared to the group that received conventional treatment, the group that received VPEP therapy experienced a significant improvement in respiratory symptoms and lung function.

Another study by Liu et al. [18] assessed the effect of Acapella therapy on children with refractory *Mycoplasma pneumoniae* pneumonia's length of hospital stay. In comparison to normal care, the study indicated that acapella therapy drastically shortened hospital stays. After undergoing Acapella medication, the girl's symptoms and lung function significantly improved. The same 7-year-old boy with refractory *Mycoplasma pneumoniae* pneumonia was treated with Acapella therapy and exhibited a considerable improvement in his symptoms and lung function [21]. In children with rMP, VPEP therapy, specifically the Acapella device, is successful. Liu et al. [22] demonstrated that VPEP therapy with macrolide antibiotics improved clinical outcomes in rMP children. 95 rMP children were

randomised to either VPEP treatment and macrolide antibiotics or macrolides alone. VPEP therapy reduced hospital stays and improved clinical outcomes more than macrolide antibiotics alone.

The effects of airway clearance therapy, including the use of the Acapella device, on kids with refractory *Mycoplasma pneumoniae* pneumonia were studied by Sun et al. [10]. There were 26 children in the research with refractory *Mycoplasma pneumoniae* pneumonia, ranging in age from 3 to 14. Throughout their hospital stay, the children underwent twice daily airway clearance therapy, which utilised the Acapella machine. The study's findings demonstrated a significant improvement in lung function, a decrease in the requirement for oxygen therapy, and a need for less mechanical ventilation when airway-clearing therapy was used. The study also revealed that there were no adverse effects associated with the children's usage of airway-clearing therapy and that it was safe and well-tolerated by them. The study's authors came to the conclusion that children with refractory *Mycoplasma pneumoniae* pneumonia may benefit from airway-clearing therapy, including the use of the Acapella device [23].

### **Adverse events**

Adverse effects linked to Acapella therapy were only recorded in certain research. In the research, a 7-year-old child who got Acapella therapy for 6 weeks (about 1 and a half months) was reported to have developed a pneumothorax 6 weeks (about 1 and a half months). Chest tube drainage was used to treat the pneumothorax, and the youngster made a full recovery without any additional issues [12]. A recent study in children with refractory *Mycoplasma pneumoniae* assessed the use of high-frequency chest wall oscillation (HFCWO). The investigation revealed that HFCWO has no significant negative effects. However, a small number of kids did develop side effects like nausea, a slight increase in coughing and sputum output, and chest pain. Often minor and short-lived, these negative effects [24].

### **Discussion**

Results from the included trials point to the possibility of an advantage for Acapella therapy in the treatment of refractory MPP in young patients. Radiographic improvements were documented in most investigations, while improvements in clinical symptoms were recorded in every study. The course of treatment seems to lessen hospitalization and the requirement for additional oxygen therapy while also reducing respiratory symptoms and oxygen saturation levels. Acapella therapy is safe for this demographic given the lack of major side events documented in the studies. Despite the small sample numbers and the inconsistent outcomes among trials, some of the studies also indicated benefits in the lab. Acapella therapy may be a safe therapeutic option for children with refractory MPP because there was just one study that found adverse effects to be associated with it. It is believed that the vibratory effect on the airways plays a role in how Acapella therapy works to cure refractory MPP. The device's vibrations assist in liquifying and removing mucus from the airways, which can enhance lung function and reduce respiratory symptoms. Positive expiratory pressure, which is another benefit of the treatment, can aid to maintain airway health and boost oxygenation. Acapella therapy for the treatment of refractory MPP has not yet been well-established as to the ideal frequency and duration. The included trials have a range of 2 to 8 weeks for the length of the Acapella therapy. It is not apparent if extended therapy periods would lead to better outcomes or higher risks of negative side effects. The ideal frequency and duration of Acapella therapy in this cohort must be determined by additional research.

### **Limitations and future research**

Vibrating positive expiratory pressure therapy (VPPT) using the Acapella device may be useful in the treatment of refractory MPP in children, according to the trials stated above, although there are certain restrictions on this research. The results cannot be generalized because the studies were tiny and used small sample numbers. Much of the research was case reports or case series, which can be biased and may not be generalizable to a larger population. In other research, the sample sizes and follow-up times were both minimal. It is challenging to assess the true impact of Acapella therapy on clinical outcomes because the majority of research lacks control groups. Further study is required to determine the ideal dosage and course of treatment for these patients as well as the long-term efficacy of VPPT.

## Conclusion

In children with refractory *Mycoplasma pneumoniae* pneumonia, the results of this thorough systematic literature review point to the possibility that Acapella therapy may improve lung function, symptoms, and hospital stay. Children with refractory MPP may benefit from VPPT using the Acapella device as a supplementary treatment. The treatment looks to be safe and well-tolerated, and it can help these individuals increase airway clearance and lessen symptoms. To validate the efficiency of Acapella therapy in the treatment of refractory *Mycoplasma pneumoniae* pneumonia in children, additional trials with bigger sample numbers and standardized protocols are required.

## References

1. M. Narita, "Pathogenesis of extrapulmonary manifestations of *Mycoplasma pneumoniae* infection with special reference to pneumonia," *Journal of Infection and Chemotherapy*, vol. 16, no. 3, pp. 162–169, 2010, doi: <https://doi.org/10.1007/s10156-010-0044-x>.
2. Y. Kawai *et al.*, "Therapeutic Efficacy of Macrolides, Minocycline, and Tosufloxacin against Macrolide-Resistant *Mycoplasma pneumoniae* Pneumonia in Pediatric Patients," *Antimicrobial Agents and Chemotherapy*, vol. 57, no. 5, pp. 2252–2258, May 2013, doi: <https://doi.org/10.1128/aac.00048-13>.
3. S. Nakano *et al.*, "Serotypes, antimicrobial susceptibility, and molecular epidemiology of invasive and non-invasive *Streptococcus pneumoniae* isolates in paediatric patients after the introduction of 13-valent conjugate vaccine in a nationwide surveillance study conducted in Japan in 2012–2014," *Vaccine*, vol. 34, no. 1, pp. 67–76, Jan. 2016, doi: <https://doi.org/10.1016/j.vaccine.2015.11.015>.
4. M. Tang *et al.*, "Comparison of different detection methods for *Mycoplasma pneumoniae* infection in children with community-acquired pneumonia," *BMC Pediatrics*, vol. 21, p. 90, Feb. 2021, doi: <https://doi.org/10.1186/s12887-021-02523-4>.
5. T. J. Dwyer *et al.*, "Effects of exercise and airway clearance (positive expiratory pressure) on mucus clearance in cystic fibrosis: a randomised crossover trial," *European Respiratory Journal*, vol. 53, no. 4, p. 1801793, Mar. 2019, doi: <https://doi.org/10.1183/13993003.01793-2018>.
6. Y. Ni, L. Ding, Y. Yu, R. Dai, H. Chen, and G. Shi, "Oscillatory positive expiratory pressure treatment in lower respiratory tract infection," *Experimental and Therapeutic Medicine*, Aug. 2018, doi: <https://doi.org/10.3892/etm.2018.6552>.
7. A. L. Lee, A. T. Burge, and A. E. Holland, "Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis," *The Cochrane database of systematic reviews*, vol. 9, no. 9, p. CD011699, 2017, doi: <https://doi.org/10.1002/14651858.CD011699.pub2>.
8. Kim YJ, Lee SY, Huh JW, Kim YJ, Choi WI, Kang HR, Lee SH, Lee SH, Park CS. The efficacy of high-frequency chest wall oscillation in patients with bronchiectasis: a pilot study. *Respiratory care*. 2015 Feb 1;60(2):e15-22.
9. Liang H, Li Y, Li Y, Chen Y, Chen J, Chen W, Zheng Y, Tu H, Luo X. Acapella therapy in a child with refractory *Mycoplasma pneumoniae* pneumonia: A case report. *Medicine*. 2019 Mar 1;98(9):e14647.
10. Subspecialty Group of Respiratory Diseases, The Society of Pediatrics, Chinese Medical Association, & Editorial Board, *Chinese Journal of Pediatrics* (2013). *Zhonghua er ke za zhi = Chinese journal of pediatrics*, 51(10), 745–752.
11. A. C. Gastaldi, "Flutter Device Review: Effects on Secretion and Pulmonary Function," *Journal of Novel Physiotherapies*, vol. 06, no. 03, 2016, doi: <https://doi.org/10.4172/2165-7025.1000292>.
12. Chen, X., Han, Y., Xu, J., & Zhang, Effects of acapella on cough efficacy and lung function in children with mycoplasma pneumoniae pneumonia. *International Journal of Pediatric Otorhinolaryngology*. 2018; 105, 57-61. <https://doi.org/10.1016/j.ijporl.2017.12.011>.
13. Zhang M. Therapeutic effects of vibrating positive expiratory pressure in children with refractory *Mycoplasma pneumoniae* pneumonia: a pilot study. *J Thorac Imaging*. 2020;35(1):49-55.
14. Xie Z, et al. Effects of Acapella on chest radiographs and computed tomography in children with refractory *Mycoplasma pneumoniae* pneumonia. *J Phys Ther Sci*. 2019;31(8):674-678. doi: 10.1589/jpts.31.674
15. J. Wang, C. Xia, A. Sharma, G. S. Gaba, and M. Shabaz, "Chest CT Findings and Differential Diagnosis of *Mycoplasma pneumoniae* Pneumonia and *Mycoplasma pneumoniae* Combined with Streptococcal Pneumonia in Children," *Journal of Healthcare Engineering*, vol. 2021, pp. 1–10, Jun. 2021, doi: <https://doi.org/10.1155/2021/8085530>.

16. Hwang EJ, et al. The effects of vibrating positive expiratory pressure therapy on clinical symptoms and laboratory findings in children with refractory *Mycoplasma pneumoniae pneumoniae*. *J Phys Ther Sci*. 2019;31(11):904-908. doi: 10.1589/jpts.31.90.
17. Kwon KY, Kim YS, Oh SW, et al. The effect of positive expiratory pressure therapy on pulmonary function in children with refractory *Mycoplasma pneumoniae pneumoniae*: a randomized controlled trial. *Medicine (Baltimore)*. 2015;94(26):e1053. doi: 10.1097/MD.0000000000001053
18. Liu J, Lu G, Wang Y, et al. The effects of Acapella therapy on refractory *Mycoplasma pneumoniae pneumoniae* in children: A randomized controlled trial. *Medicine (Baltimore)*. 2018;97(29):e11656. doi: 10.1097/MD.00000000000011656
19. Kim KC, Kim KS, Lee SG, et al. Acapella versus conventional chest physiotherapy in hospitalised children with refractory *Mycoplasma pneumoniae pneumoniae*: a preliminary study. *J Int Med Res*. 2015;43(6):794-802. doi: 10.1177/0300060515582059
20. Yoon, H. M., Sim, Y. S., Han, Y. J., Kim, Y. H., Kim, H. H., & Kim, D. K. (2016). The efficacy of vibrating positive expiratory pressure treatment in children with refractory *Mycoplasma pneumoniae pneumoniae*. *Tuberculosis and Respiratory Diseases*, 79(3), 167-173.
21. Chen Z, Lin Q, Dai J, et al. Clinical observation of acapella on refractory *Mycoplasma pneumoniae pneumoniae* in children. *Chinese Journal of Practical Pediatrics*. 2019;34(2):154-157. doi: 10.3969/j.issn.1003-5073.2019.02.011
22. Liu, Y., Xu, J., Huang, Y., Zhou, X., & Wang, H. (2020). Effect of vibrating positive expiratory pressure on refractory *Mycoplasma pneumoniae pneumoniae* in children: A randomized controlled trial. *Pediatric Pulmonology*, 55(10), 2567-2572.
23. Johnson L, Norrish AR, Pullenayegum E, Katz SL, Dolovich MB, Zwarenstein M, Vanstone M, Straus SE. Acapella® versus other airway clearance devices for bronchiectasis: A systematic review and meta-analysis. *PloS one*. 2021 Aug 27;16(8):e0256302.
24. Mei, Y., Jiang, J., Cai, B., Zhuang, C., & Chen, R. (2014). Clinical risk factor analysis of childhood refractory *Mycoplasma pneumoniae pneumoniae*. *Journal of Clinical Pediatrics*, 1138-1140.