WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 14, 902-914. Research Article ISSN 2277–7105

A COMPARATIVE STUDY ON THERAPEUTIC POTENCY OF AMBROXOL HYDROCHLORIDE VERSUS N-ACETYLCYSTINE IN THE MANAGEMENT OF LRTI AND THEIR INFLUENCE ON PROGNOSIS IN A TERTIARY CARE TEACHING HOSPITAL

Dr. Santhosh Uttangi[1], Prof. J. S. Venkatesh[2], Abhila B.*[3], Abhishek S.[3], Aksa Rajan[3] and K. Parvathi[3]

[1]Assistant Professor, S C S College of Pharmacy, Harapanahalli.

[2]Professor, S C S College of Pharmacy, Harapanahalli.

[3]Pharm D Interns, S C S College of Pharmacy, Harapanahalli.

Article Received on
29 May 2025,

Revised on 20 June 2025,
Accepted on 10 July 2025

DOI: 10.20959/wjpr202514-37605

***Corresponding Author**
Abhila B.
Pharm D Interns, S C S College of Pharmacy, Harapanahalli.

ABSTRACT

This study evaluated the effectiveness of N-Acetylcysteine (NAC) versus Ambroxol in treating Lower Respiratory Tract Infections (LRTIs), including pneumonia, COPD, tuberculosis, asthma, and acute bronchitis. 160 patients admitted to a tertiary care hospital over six months were randomly assigned to either NAC or Ambroxol. The study aimed to compare their therapeutic potency and impact on patient prognosis, utilizing the SF-36 questionnaire to assess quality of life. Results indicated that NAC demonstrated superior efficacy, with 88.75% of patients showing significant improvement compared to 75% in the Ambroxol group. NAC also resulted in faster symptom resolution and a lower incidence of side effects, with only one case of stomach discomfort compared to three in the Ambroxol group. Furthermore, patients treated with NAC experienced more pronounced improvements in quality of life across all SF-36 domains. The study concluded that NAC was more effective than Ambroxol in managing LRTI symptoms, such as cough and sputum, and in enhancing patient quality of life within one week. While acknowledging limitations, including a specific patient population and potential selection bias, the findings suggest that NAC may be a preferred treatment option for LRTIs. The study advocates for further research to confirm the broader benefits of NAC in respiratory care.

KEYWORDS: *Lower respiratory tract infection, SF36, NAC, Ambroxol Hydrochloride, COPD, Mucolytics.*

INTRODUCTION

Respiratory Tract Infection (RTI) refers to a number of infectious diseases involving respiratory tract and system. It is further classified as an upper respiratory tract infection (URTI) and lower respiratory tract infection (LRTI). URTI includes; Otitis media, Sinusitis, pharyngitis, laryngitis, rhinitis and epiglottis whereas LRTI includes; bronchitis, Bronchiolitis and pneumonia.[1] Both upper and lower respiratory tract infections are very common in developing countries like India.[2] LRTIs infections place a considerable burden on the health care system and are generally more serious than upper respiratory infections.[3]

Lower respiratory tract infections (LRTI). are infections of the airway (e.g.; bronchitis, tracheitis, and tracheobronchitis) or lung parenchyma (e.g.; pneumonia) caused by a pathogen (bacteria, viruses, or, rarely, fungi). Symptoms may include cough, fever, purulent sputum, chest pain, and shortness of breath.[4] Chest radiography (CR) is the standard diagnostic method for LRTI and it is frequently used.[5] Signs of infection on the chest X-ray were defined as: the presence of pneumonia or the presence of airways disease. The aetiological diagnosis of LRTI was based on microbiological assays. Sputum samples were used for bacterial culture, and throat swabs for viral cultures.[6] Lower respiratory tract infections (RTIs) are common conditions and their management relies on the use of prescription and over-the-counter (OTC) medicines.

Mucoactive drugs are regularly used as a therapeutic option for mucus alterations, including hypersecretion.[7] Mucoactive agents alter the viscoelastic properties of mucus and promote mucociliary clearance, and can be categorized into groups according to their mechanisms of action, including expectorants, mucoregulators, mucolytics and mucokinetics.

Ambroxol (2-amino-3,5-dibromo-N-[trans-4-hydroxycyclohexyl] benzylamine) is considered a mucoactive agent and has been widely used to treat acute and chronic respiratory diseases since 1978. It is available in multiple formulations, including lozenges, intramuscular and intravenous solutions, syrup, granules, tablets, slow-release oral formulations and nebulized solutions. Ambroxol is available OTC as a syrup. The main mechanism of action for ambroxol involves stimulation of surfactant synthesis, but that gives ambroxol effective mucokinetic and secretagogue properties, thus promoting mucous

clearance, facilitating expectoration and easing productive cough. The benefit/risk profile of ambroxol is favorable in adult patients, with a number of clinical studies reporting that ambroxol improved respiratory symptoms and prevented acute exacerbations.[8] Ambroxol may cause common side effects like nausea, vomiting stomach discomfort, dry mouth, etc.

N-Acetylcysteine (NAC) [mucolytic agent with antioxidant and anti-inflammatory] has been used worldwide for over 50 years. It has several indications and can be used in respiratory medicine [chronic obstructive pulmonary disease (COPD), interstitial lung diseases such as idiopathic pulmonary fibrosis (IPF), bronchiectasis, and influenza]. When treatment requires chronic use, as in respiratory diseases, the maximum licensed dose is 600 mg/day, usually administered once daily.[9] N-Acetylcysteine may cause side effects like blurred vision, nausea, itching, feeling of warmth etc.[10]

The **SF - 36** is referred to as a generic measure because it assesses health concepts that represent basic human values that are relevant to everyone's functional status and well – being. SF - 36 items and scales are sc ored to that a higher score indicates a better health state.[11] The SF-36 measures eight scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH).+ The **disappearance time of symptoms**, such as fever, cough, lung rale, and lung X-ray shadow was recorded in the two groups, and the efficacy was evaluated according to the standard literature. To compare the **effective rate** of the clinical treatments,

Total effective rate =[(no. of significantly effective cases+no. of effective cases)/no. of total cases]x100%.

In clinical practice, commonly used drugs for LRTI are ambroxol hydrochloride and N-acetylcysteine, which are antitussive drugs, although N-acetylcysteine is an amino acid with strong mucus dissolution. In the present study, the efficacy of ambroxol hydrochloride and N-acetylcysteine were compared in the treatment of LRTI, as well as their influence on prognosis.[13]

MATERIALS AND METHODS

Study Site: The study was conducted at the General Medicine inpatient department of Chigateri District Hospital Davangere, Karnataka over six months.

Study Design: Prospective Observational Study

Sample Size: The study was conducted over 160 inpatients of the General Medicine Department.

Study Criteria: The study was carried out by considering the following inclusion and exclusion criteria.

INCLUSION CRITERIA

- Patients of either gender.
- Patients who were prescribed with Ambroxol or N- Acetylcysteine.
- Patient admitted in Medicine department.
- Patient consented to their participation in the study by signing an informed consent form.

EXCLUSION CRITERIA

- Patients had missing and insufficient data.
- Paediatric patients.
- Pregnant and lactating women.
- Patients who were unwilling to the procedures of study.
- RVD positive patients.

STUDY PROCEDURE

- A prospective observational study was conducted on inpatients in the medical ward of Chigateri District Hospital Davangere over six months. The study received approval from the Institutional Ethical Committee of SCS College of Pharmacy. A specifically designed data collection form was created to gather information, which encompasses, the patient's demographic details, medical history, personal history, comorbid condition, social and family history as well as the medications prescribed for each individual and the patients were with the patient information leaflet and SF36 Questionnaire form for improving quality of life.

RESULTS

In this study, a total of 160 participants were enrolled and randomly assigned to two equal groups. The experimental group, consisting of 80 participants, received N- acetylcysteine [NAC], while the control group, also consisting of 80 participants, was treated with Ambroxol.

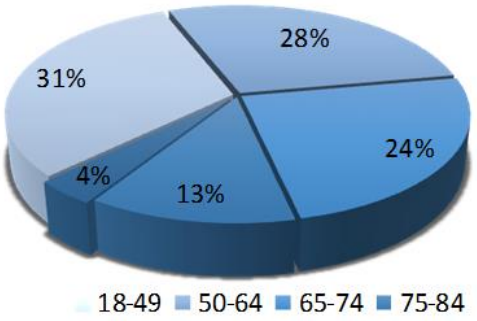
1. DEMOGRAPHIC DISTRIBUTION BY GENDER n[%]

Out of 160 participants, there were 43 male and 32 female in the experimental group and 52 male and 28 female in the control group.

GENDER	EXPERIMENTAL GROUP n[%]	CONTROL GROUP n[%]
MALE	43[53.75]	52[65]
FEMALE	32[40]	28[35]

2. DEMOGRAPHIC DISTRIBUTION BY AGE n[%]

A total of 160 participants were divided into five age groups. The largest group is those aged 18-49 years, with 50 people, making up (31.25%) of the total. The 50-64 years group follows, with 45 people (28.12%), and then the 65-74 years group, with 39 people (24.37%). The 75-84 years group includes 20 people, which is (12.5%) of the total, and the smallest group, aged 85 years and above, has 6 people, making up (3.75%).



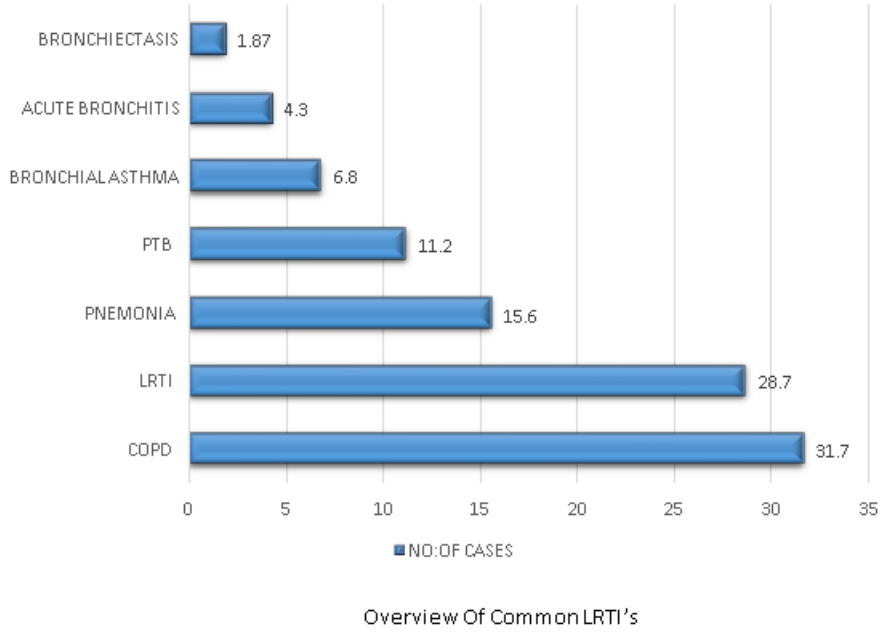
3. SMOKERS V/S NON SMOKERS BETWEEN TWO GROUPS n[%]

Out of 160 participants, 27[33.75] smokers and 53[66.2] non-smokers have been in the experimental group, while 32[40] smokers and 48[60] non-smokers have been in the control group.

SMOKING STATUS	EXPERIMENTAL GROUP	CONTROL GROUP	TOTAL
SMOKERS	27[33.75]	32[40]	59[36.8]
NON-SMOKERS	53[66.2]	48[60]	101[63]

4. OVERVIEW OF COMMON LRTI'S

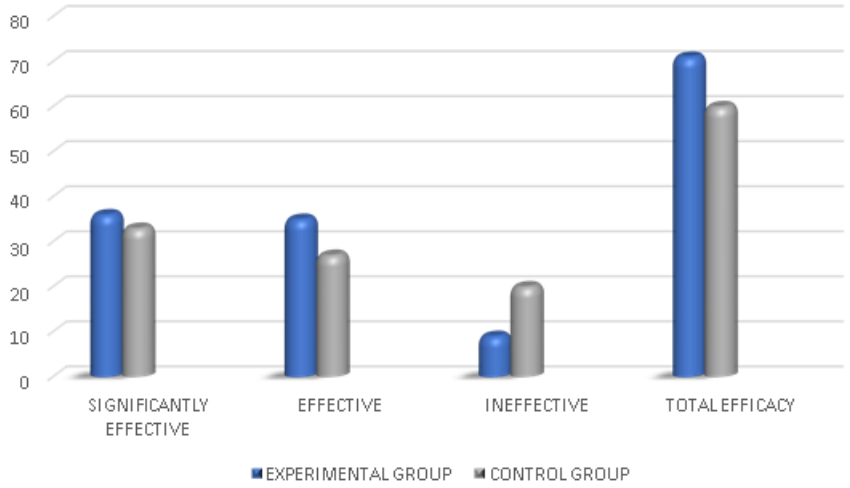
Among 160 participants, the most common lower respiratory infections (LRIs) observed were Chronic Obstructive Pulmonary Disease (COPD) with 51 cases (31.75%) and Lower Respiratory Tract Infections (LRTI) with 46 cases (28.75%). Pneumonia accounted for 25 cases (15.62%), followed by Pulmonary Tuberculosis with 18 cases (11.25%) and Bronchial Asthma with 11 cases (6.87%). Less common were Acute Bronchitis with 7 cases (4.37%) and Bronchiectasis with 3 cases (1.87%).



Overview Of Common LRTI's

5. COMPARISION OF TREATMENT EFFICACY BETWEEN TWO GROUPS n[%]

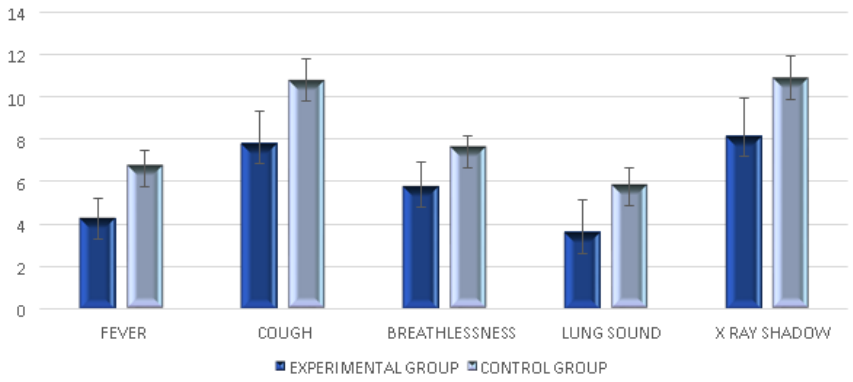
This study involved 160 participants divided into an experimental group and a control group, each containing 80 participants. In the experimental group, 36 participants (45%) experienced significant improvement, while 35 participants (43.7%) were in effective treatment, and 9 participants (11.25%) were in ineffective treatment. The total efficacy for the experimental group was 71 participants (88.75%). In the control group, 33 participants (41.25%) experienced significant improvement, 27 participants (33.7%) were in effective treatment, and 20 participants (25%) were in ineffective treatment. The total efficacy for the control group was 60 participants (75%).



6. COMPARISON OF SYMPTOMS DISAPPEARANCE TIME BETWEEN THE TWO GROUPS [Mean ±SD]

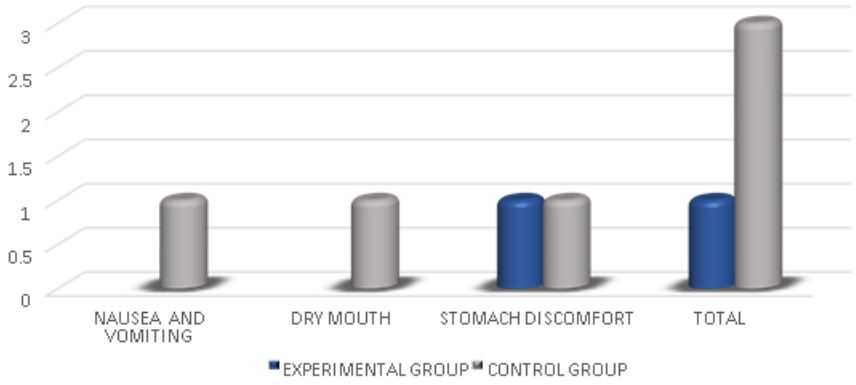
This study conducted a comparison between an Experimental Group and a Control Group, each consisting of 80 cases, to evaluate the time required for the disappearance of various symptoms. The symptoms observed were Fever, Cough, Breathlessness, Lung Sound abnormalities, and X-ray Shadow changes. In the Experimental Group, the mean time for Fever to disappear was 4.31±0.9 days, compared to 6.76±0.7 days in the Control Group. For Cough, the Experimental Group recorded a mean disappearance time of 7.83±1.5 days, whereas the Control Group took 10.78±1.02 days. Breathlessness resolved in 5.81±1.1 days in the Experimental Group, while it took 7.64±0.5 days in the Control Group. Lung Sound abnormalities disappeared in 3.63±1.52 days for the Experimental Group, compared to 5.84±0.8 days for the Control Group. Lastly, X-ray Shadow changes resolved in 8.1±1.77 days in the Experimental Group, while the Control Group took 10.9±1.02 days. The results suggest that the treatment administered to the Experimental Group was effective in significantly reducing the time for symptom resolution compared to the Control Group.

TABLE 6.6 : Comparison Of Symptoms Disappearance Time Between The Two Groups



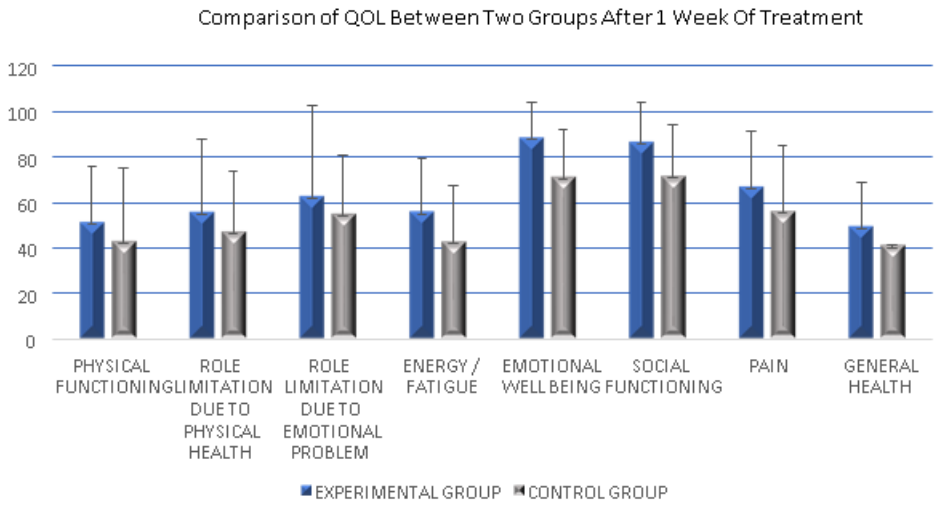
7. COMPARISON OF SIDE EFFECTS BETWEEN TWO GROUPS n[%]

This study compares the side effects between two groups, an experimental group and a control group, each consisting of 80 participants. The side effects monitored include nausea/vomiting, dry mouth, and stomach discomfort. In the experimental group, only one participant experienced stomach discomfort, resulting in a total of one side effect case. In contrast, the control group reported one case of nausea/vomiting, one case of dry mouth, and one case of stomach discomfort, totaling three side effect cases. This comparison suggests that the experimental group experienced fewer side effects overall compared to the control group.



8. COMPARISON OF QUALITY OF LIFE BETWEEN TWO GROUPS AFTER 1 WEEK OF TREATMENT [MEAN±SD]

This study's results show that after one week of treatment, the experimental group had better outcomes across all quality-of-life factors compared to the control group. For physical functioning, the experimental group scored 51.31±24.61, while the control group scored 42.93±32.31. In role limitation due to physical health, the scores were 55.78±31.85 for the experimental group and 47.18±26.80 for the control group. The experimental group also had higher scores in role limitation due to emotional problems (62.68±39.96 vs. 55.07±25.90) and energy/fatigue (56.62±23.77 vs. 42.78±24.49). Emotional well-being was notably better in the experimental group (88.57±15.39 vs. 71.47±20.91), as were social functioning (86.71±17.27 vs. 71.76±22.24), pain (66.96±24.13 vs. 56.18±28.81), and general health (49.43±19.36 vs. 41±29.05). These results suggest that the treatment provided to the experimental group significantly improved their quality of life across all measured domains compared to the control group.



DISCUSSION

Lower respiratory tract infections (LRTIs) are a significant cause of morbidity and mortality worldwide, particularly among the elderly and individuals with chronic respiratory diseases. These infections often necessitate a treatment aimed at improving mucociliary clearance and reducing bronchial secretion viscosity. N-Acetylcysteine (NAC) and Ambroxol are two widely used mucolytic agents in the management of LRTIs. NAC, recognized for its mucolytic and antioxidant properties, acts by disrupting the disulfide bonds within mucus, leading to decreased viscosity and facilitating easier expectoration. Additionally, NAC may have anti-inflammatory effects, potentially reducing the severity of respiratory symptoms. Ambroxol, on the other hand, improves mucus clearance and protects the respiratory epithelium. Ambroxol also possesses antioxidant properties and modulates lysosomal enzyme activity, which can reduce inflammation and mitigate tissue damage in the lungs.

In the present study, out of 160 participants, the result shows that LRTI was more prevalent in males than in females and 33.75 % of participants were smokers as similar to the study conducted by S. Vijay *et al.*,[14] and Ali *et al.*,[3] respectively. The reason for high risk in males of LRTI as well as COPD is attributed to smoking, use of tobacco, alcohol consumption etc. causing decreased local immunity in the respiratory tract due to defective mucociliary clearance, mucous plugging, airway collapse, respiratory muscle fatigue and the effect of medications used.

In this study, among five age group, largest group is those aged 18-49 years having 31.25% of participants, the trend similar to the study conducted by D. Weycker *et al.*,[15] Study findings indicate that rates of LRTI generally increased with older age across care settings, especially LRTI requiring hospitalization, and that, within age groups, LRTI rates were consistently higher among adults.

The most common lower respiratory tract infections observed in this study were Chronic Obstructive Pulmonary Disease (COPD) with 51 participants out of 160 participants as similar to the study conducted by R. N. Kumar *et al.*,[2] Because it causes chronic lung damage and weakens the immune system, making the lungs more susceptible to infections.

This study involved 160 participants divided into two equal groups: 80 in the experimental group receiving N-acetylcysteine (NAC) and 80 in the control group treated with Ambroxol. The total effective rate in the experimental group was 88.75%, which was higher than that in

the control group 75%. The disappearance time of symptoms such as fever, cough, shadow of the lung X-ray, time of cough disappearing and lung sound in the experimental group were shorter than those in the control group. As observed similar to that of study conducted by LIU et al.,[16] N-acetylcysteine is a derivative of acetyl group of cysteine and has a free radical scavenging effect. Because of its strong mucilage dissolving effect, N-acetylcysteine is a solution with good solubility which can be used as an expectorant. In-depth research has also revealed that: N-acetylcysteine is an antioxidant, which can effectively reduce reactive oxygen species and inhibit the activity of nuclear factor in disease-causing cells and the fiber in the concentrated sputum is cut off by the sulfhydryl group contained in the N-acetylcysteine molecule, so that the sputum is easily liquefied and removed from the body.

In this study, comparison found that the experimental group experienced fewer side effects as compared to the control group as that of study conducted by Hinkel *et al.*,[17] and N. Kuzmenko *et al.*,[18] Ambroxol has more reported side effects than N-acetylcysteine (NAC) due to its multiple mechanisms of action, which include both mucolytic and anesthetic effects, potentially leading to more diverse adverse reactions. NAC, with its more targeted mucolytic and antioxidant action, generally causes fewer side effects.

In the present study the SF-36 scoring system was also used to measure the quality of life of the two groups of patients, including the assessment of physiological functioning, pain, general health, social functioning, emotional wellbeing, role limitation due to emotional problem, energy and role limitation due to physical health. The results revealed that the patients treated with N-acetylcysteine had higher scores than the patients treated with ambroxol hydrochloride. N-acetylcysteine dissolves sputum, reduces sputum adhesion force, increases the cilia movement and inhibits the growth of pathogenic bacteria, reducing the local inflammation reaction, thus, impairing the immunity system, so that the body's humoral immunity gradually returns to normal and are similar to that of the study conducted by LIU et al.[16]

CONCLUSION

The purpose of this study was to compare the therapeutic potency of Ambroxol Hydrochloride and N-Acetylcysteine (NAC) in the management of lower respiratory tract infections (LRTIs) and to evaluate their influence on patient prognosis in a tertiary care teaching hospital.

The study involved 160 participants divided into two equal groups: 80 in the experimental group receiving N-acetylcysteine (NAC) and 80 in the control group treated with Ambroxol. The gender distribution in the study included more males than females in both the experimental and control groups. The demographic distribution by age of 160 participants, highlighting that the majority are younger, with decreasing numbers in older age groups. In the present study 36.8% are smokers. Among 160 participants, Chronic Obstructive Pulmonary Disease were the most frequently observed lower respiratory infections. The experimental group showed a higher efficacy in treatment compared to the control group, with more participants experiencing significant improvement or effective treatment. And this group had a significantly shorter mean time for the resolution of symptoms compared to the Control Group. This study found that the experimental group experienced fewer side effects as compared to the control group. The study's results indicate that after one week of treatment, the experimental group showed significant improvements in all quality-of-life factors compared to the control group, suggesting the treatment was more effective in enhancing physical and emotional well-being, social functioning, and overall health.

In summary, the present study showed that N-acetylcysteine can effectively improve the clinical symptoms and signs, and the curative effect is remarkable, suggesting that N-acetylcysteine treatment is worthy of use in hospitals. We concluded that the results of this study provide valuable information that can guide treatment decisions and potentially improve outcomes for patients with LRTIs, while also paving the way for future research to explore the long-term benefits and broader applicability of NAC in respiratory care.

ACKNOWLEDGEMENT

The authors express their gratitude to **Dr. Nagendra Rao,** the principal of SCS College of Pharmacy in Harapanahalli, for the encouragement and significant support received throughout the research.

AUTHOR'S CONTRIBUTION

All the authors have contributed equally.

CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest.

ETHICS DECLARATION

The Institutional Ethics Committee at SCS College of Pharmacy approved the protocol. All residents in the hospital provided informed consent.

CONSENT FOR PUBLICATION

All authors have consented to the publication of their work.

COMPETING INTERESTS

The authors hereby declare that they did not obtain any financial support from any source for the writing, or publication of this article.

AUTHORS FUNDING

The authors hereby declare that they did not obtain any financial support from any source for the writing, or publication of this article.

BIBLIOGRAPHY

1. DAS MS, REDDY KS, TAMKEEN MS, CHAUDHARY D, MATHEW MS. Clinical study of lower respiratory tract infections (LRTI) in pediatrics attending a tertiary care teaching hospital. International Journal of Pharmaceutical Research (09752366), Apr. 1, 2020; 12(2).
2. Kumar RN, Selva P. Analysis of prescription pattern of antibiotics among patients with respiratory tract infections at a tertiary care hospital. Biomedical and Pharmacology Journal, Sep. 25, 2019; 12(3): 1595-602.
3. Shamim M, Ali MD, Alam MS, Ali MS, Ahmad SA, Ansari MS. Drug utilization based ADRs detection of antibiotics prescribed for lrti in tertiary care teaching hospital, New Delhi. International Journal of Pharmacy and Pharmaceutical Sciences, 2018; 10(4): 7-14.
4. Fowler CL. Procalcitonin for triage of patients with respiratory tract symptoms: a case study in the trial design process for approval of a new diagnostic test for lower respiratory tract infections. Clinical infectious diseases, May 1, 2011; 52(4): S351-6.
5. Gürbüz N, Zengin N, Karaburun NC, Düzgün F, Bal A. A Comparison Study in Children with Lower Respiratory Tract Infections: Chest X-ray and Lung Ultrasound.
6. Graffelman AW, Willemssen FE, Zonderland HM, Neven AK, Kroes AC, van den Broek PJ. Limited value of chest radiography in predicting aetiology of lower respiratory tract infection in general practice. British Journal of General Practice, Feb. 1, 2008; 58(547): 93-7.

7. Zavira N, Jaelani AK, Herawati F, Yulia R. Evaluation on the use of antibiotics for pneumonia patients. Jurnal Kesehatan Prima, 2021; 15(2): 88-98.
8. NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health, InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-.
9. Wei Shen Lim. Pneumonia Overview. Classification of Pneumonia. Encyclopedia of Respiratory Medicine, 2nd edition, Elsevier, 2020; 4: 185-190.
10. Harsh Mohan. Chapter 15: The Respiratory System. Pulmonary Infections. Textbook of Pathology, seventh edition, Praveen Mohan, Tanya Mohan, Sugandha Mohan. Jaypee Brothers Medical Publishers (P) Ltd., 2015; 484-466.
11. John E. Ware. Introduction. The improvement of health status survey. SF36 health survey manual and interpretation guide. Kristin K snow. Nimrod press; 2.2-2.4.
12. Lins L, Carvalho FM. SF-36 total score as a single measure of health-related quality of life: Scoping review. SAGE open medicine, Sep. 30, 2016; 4: 2050312116671725.
13. Liu H, Wang W, Gao X. Comparison of the efficacy of ambroxol hydrochloride and N-acetylcysteine in the treatment of children with bronchopneumonia and their influence on prognosis. Experimental and therapeutic medicine, Dec. 1, 2020; 20(6): 1.
14. Vijay S, Dalela G. Prevalence of LRTI in patients presenting with productive cough and their antibiotic resistance pattern. Journal of clinical and diagnostic research: JCDR, Jan. 2016; 10(1): DC09.
15. Weycker D, Averin A, Houde L, Ottino K, Shea K, Sato R, Gessner BD, Yacisin K, Curcio D, Begier E, Rozenbaum M. Rates of Lower Respiratory Tract Illness in US Adults by Age and Comorbidity Profile. Infectious Diseases and Therapy, Jan. 2024; 13(1): 207-20.
16. Liu H, Wang W, Gao X. Comparison of the efficacy of ambroxol hydrochloride and N-acetylcysteine in the treatment of children with bronchopneumonia and their influence on prognosis. Experimental and therapeutic medicine, Dec. 1, 2020; 20(6): 1.
17. Abd El Hafiz AM, El Wakeel LM, El Hady HM. High dose N-acetyl cysteine improves inflammatory response and outcome in patients with COPD exacerbations. Egyptian Journal of Chest Diseases and Tuberculosis, Jan. 1, 2013; 62(1): 51-7.
18. El Moussaoui R, Opmeer BC, de Borgie CA, Nieuwkerk P, Bossuyt PM, Speelman P, Prins JM. Long-term symptom recovery and health-related quality of life in patients with mild-to-moderate-severe community-acquired pneumonia. Chest., Oct. 1, 2006; 130(4): 1165-72.