



Lower Respiratory Tract Infections in Primary Care, Review Article

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Any infectious illness of the upper or lower respiratory tract is classified as a respiratory tract infection (RTI). Acute bronchitis, bronchiolitis, pneumonia, and tracheitis are examples of lower respiratory tract infections (LRTIs). The most prevalent cause of death from lower respiratory infections is pneumococcal pneumonia. Pneumonia is a major cause of death globally. New advances in pneumonia diagnosis and treatment have been made, identification of new pathogens as well as the development of newer therapeutic agents like fluoroquinolones, macrolides, streptogramins, oxazolidinones, and –actam antibiotics. Despite these advancements, respiratory tract infections continue to be a challenge in both the diagnostic and therapeutic domains. Because detecting and treating pneumonia may be difficult, a number of professional organizations have created treatment recommendations. In this review we'll be looking at LRTIs and pneumonia epidemiology, etiology, diagnosis and treatment.

Keywords: Respiratory tract infections; fluoroquinolones; pneumonia; diagnosis.

1. INTRODUCTION

Any infectious illness of the upper or lower respiratory tract is classified as a respiratory tract infection (RTI). The common cold, laryngitis, pharyngitis/tonsillitis, acute rhinitis, acute rhinosinusitis, and acute otitis media are all upper respiratory tract infections (URTIs). Acute bronchitis, bronchiolitis, pneumonia, and tracheitis are examples of lower respiratory tract infections (LRTIs). In primary care, antibiotics are frequently administered for RTIs in adults and children. According to general practise consultation rates in England and Wales, a quarter of the population visits their GP each year due to an RTI. RTIs account approximately 60% of all antibiotic prescriptions in general practise [1].

Pneumonia is the sixth leading cause of mortality in the United States and a major cause of death globally. In recent years, new advances in pneumonia diagnosis and treatment have been made, including the identification of new pathogens like *Chlamydia pneumoniae*, hantavirus, and others, as well as the development of newer therapeutic agents like fluoroquinolones, macrolides, streptogramins, oxazolidinones, and –actam antibiotics. Furthermore, new diagnostic tools such as nucleic acid amplification techniques and antigen detection technologies give promise that diagnosis speed and accuracy will increase, as will therapeutic efficacy. Despite these advancements, respiratory tract infections continue to be a challenge in both the diagnostic and therapeutic domains. [2] Chronic obstructive pulmonary disease (COPD) and lower respiratory tract infections (LRTIs) are the third and fourth most prevalent causes of mortality, respectively,

after ischemic heart disease and cerebrovascular illness, according to the Global Burden of Disease 2015 report. Pneumonia, one of the most common LRTIs, with a reported annual incidence of 24.8 per 10,000 individuals. Patients between 65 and 79 years of age (63.0/10,000 people) and >80 years of age (164.3/10,000 adults) had greater rates [3].

No antibiotic prescribing, postponed (or deferred) antibiotic prescribing (in which an antibiotic prescription is written for use at a later date should symptoms worsen), and immediate antibiotic prescribing are three different antibiotic management strategies for patients with RTIs who present in primary care and other first face-to-face contact healthcare settings (such as emergency departments and walk-in centres). The choice reached by the healthcare professional and the patient is based on the healthcare professional's estimate of the danger of consequences if antibiotics are not given, as well as the patient's expectations about an antibiotic prescription. The perceived benefits of delayed prescription as a strategy over no prescribing are that it provides a "safety net" for the tiny percentage of patients who have a problem, and that a patient anticipating antibiotics is more likely to consent to this course of action than no prescribing. As a result, delayed prescribing has been promoted as a key management tool for reducing unnecessary antibiotic prescriptions [1]. Identifying particular etiologic agents makes it easier to choose the best pathogen-directed antibiotic treatment and to accurately stage the disease. By focusing on antibiotic selection, one can avoid the negative implications of injudicious use, such as higher costs, antibiotic resistance, and side effects. Furthermore, if a cause is identified, transitioning

from an empiric broad-spectrum intravenous regimen to a narrower-spectrum oral regimen is easier. Antibiotics with a smaller scope of action are frequently less costly than antibiotics with a broad spectrum of action. The second objective for establishing an aetiology is to obtain more epidemiologic data that may be used to improve care for other patients by expanding the body of knowledge. Improved epidemiologic data aids in the detection of new infections, drug-resistant organisms, and trends. It also aids in the reduction of antibiotic misuse [2].

Antibiotic prescription puts people at risk of side effects, pushes people to seek care for (mostly) self-limiting diseases, and puts both people and society at risk of antibiotic resistance. Many general practitioners may not associate their own prescribing habits with rising antibiotic resistance, viewing resistance as primarily a hospital-based issue. Antibiotic prescription varies widely across Europe and the United Kingdom, with little evidence that this is linked to differences in illness spectrum or complication rates [4-10].

2. EPIDEMIOLOGY

The most prevalent cause of death from lower respiratory infections is pneumococcal pneumonia. Pneumococcal pneumonia is the most frequent cause of pneumonia, according to the GBD 2015 research, accounting for nearly 15 lakh premature deaths worldwide in 2015. Children under the age of five are particularly vulnerable, and LRTIs are the leading cause of mortality in this age group. In the outpatient environment, community-acquired pneumonia (CAP) and acute exacerbation of chronic bronchitis (AECB) are the two most prevalent acute LRTIs. The yearly incidence of CAP is estimated to be between 5 and 11 per 1,000 people, with greater rates in the older population. It is the primary cause of death from infectious illnesses in affluent nations and a substantial source of morbidity and mortality in poor countries, with enormous medical expenses, topping 10 billion u.s. dollars alone each year [3].

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3. ETIOLOGY

Streptococcus pneumoniae, *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Haemophilus influenzae* are common bacterial infections that cause conventional pneumonia, whereas *Legionella pneumophila*, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, and *Chlamydia psittaci* cause atypical CAP. In many cases, *S. pneumoniae* is the major cause of CAP. Pneumococcus was formerly the most often reported bacterial infection in the United States, but it currently only affects 10%–15% of inpatients. According to data from Western nations, *S. pneumoniae* is found in 24 percent–45 percent of patients with CAP and severe CAP [3,11-14].

The increase of neutrophils and a plasma exudate outside the blood vessels characterise acute inflammation. Neutrophils move out of the pulmonary capillaries and into the air spaces during pulmonary infection. Neutrophils use reactive oxygen species and antimicrobial proteins to destroy ingested microorganisms after phagocytosis. The neutrophil extracellular trap is another microbicidal route that has been discovered (NET). Neutrophils eject NETs, which are made up of a chromatin meshwork carrying antimicrobial proteins and catch and destroy microorganisms outside the cell. Deficits in neutrophil number (neutropenia) and quality (e.g., chronic granulomatous illness) as well as impairments in complement and immunoglobulins predispose individuals to opportunistic lung infections. Acute inflammation can be considered a critical innate immune response in the lungs because neutrophils and plasma proteins mediate innate immune processes and are required to avoid lung infection [15].

In a study that looked at the causative agent of infection in primary care for lower respiratory tract infection. In 59 percent of cases, a probable pathogen was found (11 percent of bacterial pathogens, 38 percent of viral pathogens, and 10% of both bacterial and viral pathogens). *S. pneumoniae* (5.5 percent overall, 9.2 percent in CAP patients) and *H. influenzae* were the most prevalent bacterial infections detected (5.4 percent overall, 14.2 percent in CAP patients). *S.*

pneumoniae were extremely resistant to penicillin in less than 1% of cases, while 12.6 percent of H. influenzae were -lactamase positive. Human rhinovirus (20.1%), influenza viruses (9.9%), and human coronavirus were the most prevalent viral infections found (7.4 percent). Human influenza virus, human parainfluenza virus, and human respiratory syncytial virus, as well as human rhinovirus, human coronavirus, and human metapneumovirus, were found in LRTI patients at much higher rates than in controls [16].

another study was done to look at the aetiology and prediction of pneumonia in patients with a lower respiratory tract infection in primary care. In this study Pneumonia was confirmed radiographically in 48 of 364 individuals (13 percent). Individuals with pneumonia had a higher rate of bacterial infection (33 percent versus 17 percent), but non-pneumonic patients had a higher rate of viral infection (26 percent versus 13 percent). Hospitalization was more likely in individuals with pneumonia compared to non-pneumonic patients (19% vs. 3%), as well as in patients with pneumococcal infection vs. non-pneumonic patients (26 versus 4 percent). In Conclusion, The most prevalent bacterial pathogen was Streptococcus pneumoniae. Patients with pneumonia or pneumococcal infection had the highest likelihood of hospitalisation [17].

4. CLINICAL PRESENTATION AND DIAGNOSIS

Because detecting and treating pneumonia may be difficult, a number of professional organisations have created treatment recommendations to provide doctors with criteria for diagnosis and illness management. The American Thoracic Society (ATS), the British Thoracic Society, and the Canadian Infectious Disease Society all released treatment recommendations for community-acquired pneumonia in 1993 [2].

Based on the patient's appearance, clinical findings, causative microorganisms, and illness history, pneumonia can be characterised as "atypical" or "typical." The course of atypical pneumonia differs slightly from that of conventional pneumococcal pneumonia. Aside from that, there are numerous clinical similarities between normal and atypical pneumonia. Acute fever, chills, pleuritic chest pain, and a productive cough are all symptoms of typical pneumonia, whereas myalgias, fever without chills,

headache, and an unproductive cough are all symptoms of atypical pneumonia [3,18,19].

The patient's medical history aids in the identification of particular risk factors and illnesses linked to certain infections. For example, pneumonia might be caused by S. pneumoniae, Klebsiella pneumoniae, or anaerobic bacteria in a patient with a history of drinking. Human immunodeficiency virus (HIV) infection may raise concerns about infections caused by S. pneumoniae, Mycobacterium tuberculosis, Pneumocystis carinii, and other opportunistic pathogens, depending on the stage of infection.

The IDSA recommends using chest radiography to identify pneumonia and distinguish individuals with acute febrile bronchitis from those who have pneumonia. The chest x-ray may identify and measure lung illness, assess the severity and extent of pneumonia, and offer a baseline from which to assess clinical response, in addition to aiding in the diagnosis of pneumonia. A physical examination will not be able to confirm a pneumonia diagnosis. It does, however, aid in determining the severity of the condition and determining the best treatment location [2].

5. MANAGEMENT

Antibiotic prescribing trends for RTIs differ greatly amongst general practises. Although delayed and no prescription tactics have been recommended since the late 1990s, it is unknown how widely they are used in primary care. In the United Kingdom, there is presently no national clinical guideline on antibiotic prescribing in primary care for RTIs that are expected to resolve on their own. As a result, primary care and other first-contact healthcare workers (GPs, nurse practitioners, pharmacists, and those who work in emergency rooms) require instruction on which RTIs do not require immediate antibiotic treatment and which antibiotic management strategies could be offered once it is determined that the patient does not require immediate antibiotic treatment the clinical and cost effectiveness of delayed prescribing or no prescribing as management strategies during the consultation to ensure the appropriate use of antibiotics for RTIs [1].

Doxycycline, a macrolide (azithromycin, clarithromycin, or erythromycin), or a newer fluoroquinolone with increased anti-S. pneumoniae activity are the IDSA-preferred

empiric therapy options for outpatients with CAP. It's also worth noting that regional susceptibility statistics should be considered when prescribing antibiotics, and that penicillin-resistant *S. pneumoniae* may also be resistant to doxycycline and macrolides [2].

In outpatients, amoxicillin is the chosen antibacterial medication for early empiric treatment. Patients with penicillin hypersensitivity should take macrolides (clarithromycin and azithromycin). Antimicrobials such as fluoroquinolones, when used incorrectly, can raise the chance of fluoroquinolone-resistant *M. tuberculosis*. There's also the possibility of hiding active TB. In light of this issue, Indian guidelines recommend that patients with CAP get macrolides such as clarithromycin/azithromycin instead of quinolones/doxycycline as initial empiric treatment. Doxycycline is not advised for the treatment of CAP due to extensive resistance among bacteria that cause it [3].

The ATS divides CAP patients into those who have modifying variables (such as cardiopulmonary illness) and those who don't. The ATS advises monotherapy with a macrolide or doxycycline in individuals who do not have modifying variables. They propose either a combination treatment with a -lactam and a macrolide or monotherapy with an antipneumococcal fluoroquinolone in patients with modifying variables. The ATS did remark, however, that newer fluoroquinolones had enhanced pneumococcal coverage and enable once-daily dosage for gram-positive, gram-negative, and atypical bacteria [2].

COPD is a chronic inflammatory disease. In addition, infections can amplify the inflammatory response during acute exacerbations. Antibiotics such as macrolides (clarithromycin/azithromycin) are among the options for treating simple COPD. Macrolides are effective for individuals who have no risk factors, no heart illness, are 65 years old, have a FEV1 more than 50% expected, and have had three exacerbations in a year [3].

The American Thoracic Society ranked the currently available antipneumococcal fluoroquinolones according to their antipneumococcal activity (moxifloxacin >gatifloxacin >levofloxacin), noting that gemifloxacin, an investigational fluoroquinolone, is more active against *S. pneumoniae* than moxifloxacin or gatifloxacin. Although these in vitro discrepancies may not be clinically meaningful at this time, the ATS cautioned that

they might lead to future disparities in clinical success and resistance rates [2].

In a study Antibiotics' efficacy has been studied in randomised controlled trials. In England, 56 general practises. Children aged 6 months to 12 years who presented to primary care with acute uncomplicated LRTI were included in the study. Patients were randomly randomised to take amoxicillin 50 mg/kg per day in a 1:1 ratio. The antibiotics and placebo groups had equal median durations of moderately poor or worse symptoms (6 days in the antibiotics group vs. 6 days in the placebo group). In the five designated clinical groupings, there were no differences in the main outcome between the therapy groups (patients with chest signs, fever, physician rating of unwell, sputum or chest rattle, and short of breath). Amoxicillin is unlikely to be clinically helpful for simple chest infections in children, either overall or in critical subgroups for whom antibiotics are often recommended. Unless pneumonia is suspected [20].

6. CONCLUSION

Acute bronchitis, bronchiolitis, pneumonia, and tracheitis are examples of lower respiratory tract infections (LRTIs). Pneumonia however is the most serious condition of LRTIs, even with current advancement in treatment and diagnosis methods. Antibiotic resistance is major challenge for clinicians worldwide, some studies suggest that using antibiotic in some cases doesn't improve overall progression, with that being said antibiotic usage should follow guidelines whenever it's possible to reduce side effects and also reduce causing of resistance.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Centre for Clinical Practice at NICE (UK). Respiratory Tract Infections - Antibiotic

- Prescribing: Prescribing of Antibiotics for Self-Limiting Respiratory Tract Infections in Adults and Children in Primary Care. London: National Institute for Health and Clinical Excellence (UK); 2008. (NICE Clinical Guidelines, No. 69.) Available:<https://www.ncbi.nlm.nih.gov/books/NBK53632/>
2. Limper AH. Overview of Pneumonia. *Goldman's Cecil Medicine*. 2012;587-596. DOI: 10.1016/B978-1-4377-1604-7.00097-X
 3. Mahashur A. Management of lower respiratory tract infection in outpatient settings: Focus on clarithromycin. *Lung India*. 2018;35(2):143-149. DOI: 10.4103/lungindia.lungindia_262_17 PMID: 29487250; PMCID: PMC5846264.
 4. Stanton N, Francis NA, Butler CC. Reducing uncertainty in managing respiratory tract infections in primary care. *Br J Gen Pract*. 2010;60(581):e466-75. DOI: 10.3399/bjgp10X544104. PMID: 21144191; PMCID: PMC2991763.
 5. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Ther Adv Drug Saf*. 2014;5(6):229-241. DOI: 10.1177/2042098614554919
 6. Simpson SA, Wood F, Butler CC. General practitioners' perceptions of antimicrobial resistance: a qualitative study. *J Antimicrob Chemother*. 2007;59(2):292–296.
 7. Butler CC, Hood K, Verheij T, et al. Variation in antibiotic prescribing and its impact on recovery in patients with acute cough in primary care: prospective study in 13 countries. *BMJ*. 2009;338:b2242.
 8. Van Duijn HJ, Kuyvenhoven MM, Butler CC, et al. Variation in outpatient antibiotic use in three European countries: exploration of possible determinants. *Eur J Gen Pract*. 2005;11(3–4):139–140.
 9. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. *P T*. 2015; 40(4):277-283.
 10. Wang KY, Seed P, Schofield P, et al. Which practices are high antibiotic prescribers? A cross-sectional analysis. *Br J Gen Pract*. 2009;59(567):315–320.
 11. Woodhead M, Blasi F, Ewig S, Garau J, Huchon G, Ieven M, et al. Guidelines for the management of adult lower respiratory tract infections – Summary. *Clin Microbiol Infect*. 2011; 17(Suppl 6):1–24.
 12. Cunha BA. The atypical pneumonias: Clinical diagnosis and importance. *Clin Microbiol Infect*. 2006;12(Suppl 3):12–24.
 13. Musher DM, Thorner AR. Community-acquired pneumonia. *N Engl J Med*. 2014;371:1619–28.
 14. Khawaja A, Zubairi AB, Durrani FK, Zafar A. Etiology and outcome of severe community acquired pneumonia in immunocompetent adults. *BMC Infect Dis*. 2013;13:94.
 15. Mizgerd JP. Acute lower respiratory tract infection. *N Engl J Med*. 2008;358(7):716-27. DOI: 10.1056/NEJMra074111. PMID: 18272895; PMCID: PMC2711392.
 16. Ieven M, Coenen S, Loens K, Lammens C, Coenjaerts F, Vanderstraeten A, Henriques-Normark B, Crook D, Huygen K, Butler CC, Verheij TJM, Little P, Zlateva K, van Loon A, Claas ECJ, Goossens H. Aetiology of lower respiratory tract infection in adults in primary care: a prospective study in 11 European countries, *Clinical Microbiology and Infection*. 2018;24(11): 1158-1163. ISSN 1198-743X, Available:<https://doi.org/10.1016/j.cmi.2018.02.004>.
 17. Holm A, Nexoe J, Bistrup LA, Pedersen SS, Obel N, Nielsen LP, Pedersen C. Aetiology and prediction of pneumonia in lower respiratory tract infection in primary care. *Br J Gen Pract*. 2007;57(540):547-54. PMID: 17727747; PMCID: PMC2099637.
 18. Prasad R. Community acquired pneumonia: Clinical manifestations. *J Assoc Physicians India*. 2012;60(Suppl): 10–2.
 19. Bedi RS. Community acquired pneumonia-typical or atypical? *Lung India*. 2006;23:130–1.
 20. Little P, Francis NA, Stuart B, O'Reilly G, Thompson N, Becque T, Hay AD, Wang K, Sharland M, Harnden A, Yao G, Raftery J, Zhu S, Little J, Hookham C, Rowley K, Euden J, Harman K, Coenen S, Read RC, Woods C, Butler CC, Faust SN, Leydon G,

Wan M, Hood K, Whitehurst J, Richards-Hall S, Smith P, Thomas M, Moore M, Verheij T. Antibiotics for lower respiratory tract infection in children presenting in primary care in England (ARTIC PC): A double-blind, randomised,

placebo-controlled trial. *Lancet*. 2021; 398(10309): 1417-1426.

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