Original Research

The impact of adherence to community-acquired pneumonia (CAP) management guidelines on improving clinical outcomes in hospitalized patients

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Abstract

Objectives: Community-acquired pneumonia (CAP) is linked with high morbidity and mortality, particularly among the elderly. Because of the high incidence and accompanying financial expenses, accurate diagnosis and adequate care of this group hospitalized with CAP are required. The purpose of the study was to assess the level of adherence to CAP national guidelines at a private hospital, as well as the impact of adherence to these national recommendations on clinical outcomes. **Methods:** Data from electronic medical records of adult patients hospitalized with CAP between 2018 and 2019 were retrieved for a quantitative observational retrospective cohort research. **Results:** This study comprised 159 patients, with 76 patients (47.8%) receiving therapy according to the recommendations of the guidelines. A total of 75 (98.7%) of those patients were hospitalized across the ICU wards. In contrast, 98.4% (64/65) of patients who had received empiric antibiotic treatment within isolation floors were non-compliant. There was a statistically significant relationship between the level of adherence to CAP clinical guidelines and the following variables: The 72-hour reassessment (P = 0.01), medications altered OR retained when culture findings were revealed (P = 0.01), primary diagnosis (P = 0.028), and total intended period of antibiotic therapy (P = 0.007). **Conclusions:** According to the findings of this study, higher adherence to the guidelines amongst ICU patients was linked to better outcomes, such as a significant reduction in the overall planned period of antibiotic therapy.

Keywords: Community-acquired pneumonia (CAP); cohort study; adherence; Jordan

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INTRODUCTION

Community-acquired pneumonia (CAP) is distinct from hospital-acquired pneumonia (HAP) in that it is a lung parenchymal infection acquired in the community. CAP is often accompanied by new radiographic infiltration as well as usual clinical signs.[1,2] In developed countries, CAP affects roughly 5.6- 6.11 per 1000 adult population each year, making it one of the top causes of mortality from infectious illness and spending a significant portion of health resources.[3-5] CAP primarily affects the elderly and those with numerous comorbidities.[4,6-14] Streptococcus pneumonia, Mycoplasma pneumonia, Chlamydophila pneumonia, and respiratory viruses are the most common etiologic agents responsible for CAP.[36] The most common etiologic agent responsible for CAP in both hospitalized patients and patients in the community is S. pneumonia.[37] Although Staphylococcus aureus is currently considered an infrequent cause of CAP, it is linked with a more severe clinical presentation.[1,2,15-19] These guidelines were shown to improve the quality of care when applied in ordinary clinical practice.[6,7] Improving clinical outcomes and reduction of healthcare costs is the main objective of the guidelines, which can be achieved by adapting national guidelines to different local settings and evaluating compliance (local implementation).[6,7]

In this scenario, "Specialty Clinic Hospital" followed national recommendations for CAP therapy. The use of pneumonia severity assessment tools and adherence to treatment guidelines will enhance concordant antibiotic prescriptions for CAP patients.[1,2] To improve adherence to treatment guidelines, they must be given in a user-friendly and easily accessible style, accompanied by a multifaceted educational intervention that is connected with the Antimicrobial Stewardship Program (ASP).[1,2] Adherence to evidence-based CAP recommendations has been demonstrated to have a dramatic and beneficial influence on both patients' clinical outcomes and healthcare costs,[20] and a decrease in length of stay (LOS) with a favourable impact on mortality.[1-3,7,20,21]

The purpose of the current study was to assess the level of adherence of physicians to CAP national guidelines at a private hospital and to measure the impact of adherence on clinical outcomes including reduction of length of stay and duration of antimicrobial therapy.

METHODS

Study design and population

A quantitative observational retrospective cohort study was conducted at a private hospital over two years (from January 2018 to December 2019) in Jordan. Because of its unique position in the heart of Jordan's capital, Amman Specialty Hospital employs over 300 professionals who are linked with various clinical service lines and specializations such as medicine, obstetrics, paediatrics, surgery, and critical care services that support the trauma program, as well as the country's largest burn unit.

The study population included adult (≥ 18 years) immune-competent hospitalized patients with CAP diagnosis with no history of hospitalization within 90 days prior to admission. The onset of symptoms should have occurred before or at least up to 48 hours after admission. Pregnant women were excluded from the study.

Adult patients hospitalized with CAP (N=159) were selected per the inclusion criteria. The population sample has been divided into two groups:

  I. Cohort 1- nonadherent group (NAG): a sample that did not conform to Specialty Hospital National CAP clinical guidelines
  II. Cohort 2 - adherent group (AG): a sample that followed Specialty Hospital National CAP clinical guidelines.

Ethics approval

All procedures performed in this study were in compliance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The approval was obtained from the Institutional Review Board (IRB) at Specialty Hospital (Reference No: 103772/T/1/5). Due to the retrospective design, formal patient consent was waived by IRB.

Data collection

Data were extracted from electronic medical records of admitted adult immune-competent patients diagnosed with CAP. The decision for hospitalization was at the discretion of the Emergency department (ED) physician. Following the hospital's electronic medical records software and the disease control and prevention (CDC) assessment tools for the appropriateness of antibiotics for CAP, data has been reviewed and documented as presented in Tables 1 and 2. Demographic and clinical data were collected from hospital files including age, gender, initial antibiotic, choice of antibiotic, 72 hours reassessment, primary diagnosis, antimicrobial therapy, CURB 65 score, planned duration, and length of hospital stay.

DEFINITIONS

Community-acquired pneumonia (CAP) was defined as an acute infection of the lower respiratory tract in patients who had lived outside the hospital for at least 90 days prior to admission to the study hospital.

Length of stay (LOS): This variable was assessed in days from the time of admission to the time of release (or censoring). These timings were recorded in the patient's electronic medical record.

Duration of antibiotic therapy (DOH): the total number of days of all antibiotics that the patient received while in the hospital and after discharge.

Outcome measures

The primary outcome: was the physicians' level of adherence to "Specialty Hospital" National CAP guidelines.

Secondary outcome: was the association relationship between adherence to guidelines and the clinical outcomes such as reduction of LOS and duration of antimicrobial therapy.

Statistical analysis

The T-test and chi-square were used as statistical tools to assess the relationship between the variables and adherence level to guidelines. Categorical variables such as patient gender, medical service/specialty, initial given antimicrobial agent, antimicrobial choice within the admission wards, 72-hour reassessment, and main diagnosis were analyzed using the Chi-Square test. Continuous variables such as patient age, CURB 65 score, anticipated duration, and LOS were analyzed using the T-test. SPSS (version 25) software was used to analyze collected data. All tests are two-sided, and statistical significance was set at p-value < 0.05.

RESULTS

Incidence of CAP and level of Physician adherence to CAP national guidelines

In this study, 284 patients with CAP diagnoses from 2018 and 2019 were collected. Of those, 125 were excluded as per exclusion criteria. In about half 47.5% (n=76) of cases, the selection of medication regimens by physicians was compliant with national clinical standards, of which 75 (98.7%) patients were hospitalized across the ICU wards and only one patient

(1.3%) was admitted to the isolation floors of the studied hospital.

Patient demographic and baseline characteristics

As shown in Table 1, the majority of patients were males (55.3%) with a mean age of 52.3. Analyzed data in Table 2 has revealed that the most common medical specialty for prescribing physicians was general medicine for both groups (81.0% and 82.50%); with the least common being general surgery (4.70%, 2.90%); respectively. The 72-hour reassessment was done on 120 patients, of which 76 were properly conducted as per guidelines. Overall, in the AG, the percentage of cases where the organism was found to be susceptible to the initially prescribed antibiotic was higher than in NAG, with values of (22.5% and 13.1%), respectively. According to the results, the most commonly prescribed antibiotic in NAG was piperacillin/ tazobactam, while quinolones were the most common in AG. A significant lowering in the average total planned duration of antibiotic therapy was observed in the AG compared to NAG (3.7 vs 4.9 days), respectively. In both groups, influenza/ pneumonia was the most common primary diagnosis (42.6% and 66% for NAG and AG, respectively), with UTI being the least frequent (3.7% and 3.8%), respectively.

Univariable analysis results

The results of the univariable analysis are displayed in Table 2. There was no statistically significant relationship between the level of adherence to CAP clinical guidelines and the following variables: Gender (P = 0.556), type of medical service specialty (P = 0.500), the susceptibility of the isolated organism by culture to the prescribed antibiotic (P = 0.068), age (P = 0.072), CURB 65 score (P = 0.575) and LOS (P = 0.662). The following variables had a significant relationship with the level of adherence to CAP clinical guidelines: Initial antibiotic regimen (P = 0.01), the 72 hours reassessment (P value = 0.01), whether antibiotics were switched after culture results were available (P = 0.01), primary diagnosis (P = 0.028), antibiotic therapy (P=0.030) and total planned duration of antibiotic (P = 0.007).

S.N	Variable		No of Samples (159)
	Table 1. Demographic data for all samples		
1	Age, mean (SD), years		52.3 (22.05)
2	CURB 65 Score, mean (SD)		2.1 (0.31)
3	Total planned duration of antibiotics, mean (SD), days		4.3 (2.21)
4	Length of stay, mean (SD) days		7 (10.6)
5	Gender, n (%)	Female	71 (44.7%)
		Male	88 (55.3%)
6	Medical speciality, n (%)	• Medicine-General	130 (81.8%)
		• Surgery-General	6 (3.8%)
		• Critical Care	23 (14.4%)
7	Initial antibiotics were consistent with Specialty Hospital guidelines, n (%)	• Isolation Floors	65 (40.9%)
		• ICU	94 (59.1%)
8	72-hour reassessment occurrence, n (%)	• No	39 (24.5%)
		• Yes	120 (75.5%)
9	Organism isolated by culture was susceptible to the prescribed antibiotic, n (%)	• No	131 (82.4%)
		• Yes	28 (17.6%)
10	Antibiotics switched after culture results were available, n (%)	• No	83 (52.2%)
		• Yes	76 (47.8%)
11	Primary diagnosis, n (%)	• Influenza/Pneumonia	85 (53.5%)
		• Other Bacterial Diseases	22 (13.8%)
		• Urinary tract diseases	6 (3.8%)
		• Other diseases	46 (28.9%)
12	Antimicrobial therapy	• Quinolones	81 (50.9)
		• Piperacillin Tazobactam	34 (21.4)
		• Cephalosporins	17 (10.7)
		• Carbapenems	50 (31.4)
		• Others	26 (16.4)

Table 2. Univariate analysis results

S. No	Variable No (n= 83)		Adherence to guidelines		P Value
			No (n= 83)	Yes (n= 76)	
1	Age, mean (SD), years		41.0 (23.54)	63.5 (20.52)	0.072
2	CURB 65 Score, mean (SD)		2.1 (0.38)	2.1 (0.23)	0.575
3	Total planned duration of antibiotics, mean (SD), days		4.9 (2.14)	3.7 (2.28)	0.007
4	Length of stay, mean (SD) days		6.2 (7.48)	7.5 (13.77)	0.662
5	Gender, n (%)	Female	37 (44.4%)	34 (41.5%)	0.556
		Male	46 (55.6%)	42 (58.5%)	
6	Medical speciality, n (%)	• Medicine-General	67 (81.0%)	63 (82.5%)	0.500
		• Surgery-General	4 (4.7%)	2 (2.9%)	
		• Critical Care	12 (14.3%)	11 (14.6%)	
7	Initial antibiotics were consistent with Specialty Hospital guidelines, n (%)	• Isolation Floors	64 (77.1%)	1 (1.0%)	0.010
		• ICU	19 (22.9%)	75 (99.0%)	
8	72-hour reassessment occurrence, n (%)	• No	39 (46.4%)	0 (0.0%)	0.010
		• Yes	44 (53.6%)	76 (100.0%)	
9	Organism isolated by culture was susceptible to the prescribed antibiotic, n (%)	• No	72 (86.9%)	59 (77.5%)	0.068
		• Yes	11 (13.1%)	17 (22.5%)	
10	Antibiotics switched after culture results were available, n (%)	• No	65 (77.9%)	18 (23.8%)	0.010
		• Yes	18 (22.1%)	58 (76.2%)	
11	Primary diagnosis, n (%)	• Influenza/Pneumonia	35 (42.6%)	50 (66.0%)	0.028
		• Other Bacterial Diseases	18 (22.2%)	4 (5.7%)	
		• Urinary tract diseases	3 (3.7%)	3 (3.8%)	
		• Other diseases	27 (31.5%)	19 (24.5%)	
12	Antimicrobial therapy	• Quinolones	5 (5.4)	76 (66.1)	0.030
		• Piperacillin Tazobactam	34 (36.6)	0 (0.0)	
		• Cephalosporins	17 (18.3)	0 (0.0)	
		• Carbapenems	15 (16.1)	35 (30.4)	
		• Others	22 (23.7)	4 (3.5)	

DISCUSSION

The preservation of antimicrobial drugs for severe and life-threatening illnesses is critical especially with the emergence of opportunistic pathogens of CAP infections as a result of widespread improper implementation of these medicines.[20,23-28] Recognizing that the cost of CAP in the inpatient treatment context is roughly 25 times higher than in the outpatient, the risk of thromboembolism and superinfection by more vicious or resistant hospital pathogens is growing in hospitalization.[3,29-34] CAP was chosen for the observational research in this investigation because it accounts for a high fraction of hospital antibiotic consumption in the Specialty Hospital.

This study identified seven variables that have no significant relationship with the level of adherence to clinical guidelines including gender, type of medical service specialty, the choice of antibiotic regimen (Isolation floors, ICU wards), the susceptibility of the isolated organism by culture to the prescribed antibiotic, age, CURB 65 score, and LOS. LOS was predicted to be connected to the degree of adherence,

which was not seen in our study, and this might be due to administration rather than clinical variables such as receiving approval, finishing documentation, admission and discharge plan provided by the physician, and factors related to patients such as the patient refused to be discharged or no one arrived from a family member to take the patient home.

In addition, six significant variables' relationship with the level of adherence was shown including the initial antibiotic regimen, the 72 hours reassessment, whether antibiotics were switched after culture results were available, primary diagnosis, antibiotic therapy, and total planned duration of antibiotic. This study determined the total planned duration of antibiotics in Cohort 1 (mean = 4.9 days) versus 2 (mean = 3.7 days) in the other group; an obvious reduction in the total planned duration of antibiotics occurred when the treatment regimen adhered to the guidelines.

This study helps in determining the areas of improvement to enhance the level of adherence to ASP. The initial antibiotic regimen can be considered an essential area for improvement

in isolation floors as around 64 (98.5%) patients had initial antibiotics inconsistent with the Specialty Hospital guidelines, so we recommend keeping continuous monitoring to assure awareness of the team and proper adherence across the studied hospital isolation floors. Another essential area of improvement is the 72 hours reassessment (whether an organism is isolated by the culture within 72 hours of the first dose of antibiotics, and if a documentation review has been done). There were around 39 patients from the total sample size whose 72-hour reassessment was missed and 44 patients who had an improper 72-hour reassessment done leading to a lack of adherence to the guidelines. Such variables have a significant relationship with the level of adherence to the introduced clinical guidelines in the isolation floors during the study period, so continuous monitoring aligned with ongoing awareness sessions, and friendly-user guidelines will dramatically enhance the level of adherence.

Whether antibiotics were switched after culture results were available is another essential area of improvement, as there were 72 patients from the total sample whose antibiotics weren't changed after culture results were available, in which the prescribed and dispensed antibiotics were inconsistence with the guidelines. Of the 18 patients whose antibiotics were changed after culture results were available, it was changed into an improper antibiotic that wasn't matched with the culture result, and such practice will enhance the trend of antibiotic resistance, minimize clinical outcomes and increase healthcare costs in all dimensions.

The influence of CAP clinical recommendations on patient outcomes was previously evaluated in Italy.[20] The findings in both, retrospective and prospective, studies were positive showing a statistically significant reduction in the failure rate and mortality rate in the guideline-recommended therapies compared to non-compliant therapies.[20] Another retrospective research in Brazil found that patients who were treated per the criteria for hospitalization and antibiotic therapy in accordance with the guidelines had shorter hospital stays.[21] Furthermore, a prospective study in Athens sought to determine whether pulmonologists followed both the revised practice recommendations issued by the IDSA in 2003 and the Greek national clinical CAP guidelines.[20] This study verified the reduction in LOS when patients follow the same revised guidelines.[20] Moreover, the introduction of CAP clinical practice guidelines in Spain indicated a significant improvement in both the treatment process and the clinical outcomes in CAP patients.[20] The lack of applicability of these guidelines to the general population was one of the key drawbacks of the clinical studies that were examined.[1,2,3,7,10,21,22]

A multicenter stewardship initiative has been recently evaluated for its impact on antibiotic duration of therapy (DOT) in hospitalized CAP patients. The DOT was reduced from 9 to 6 days (p<0.001), without negatively impacting the clinical outcomes.[38] Another retrospective study was done on veterans hospitalized with pneumonia to assess the impact of the ASP on clinical outcomes. It was shown to reduce the duration of therapy and length of stay, and lower rates of

readmission and Clostridium difficle infections within 30 days.[39] In Canada, a larger retrospective study was carried out on CAP adult patients. It was shown that mortality rates were lower when treatment was concordant with the guidelines (6% vs 10% when non-compliant, p<0.001).[40] A recent retrospective observational study was carried out in Hungary to assess the impact of adherence to guidelines on CAP patients. The 30-day mortality rate was slightly lower in the guideline-adherent group than in non-adherent to national guidelines.[41]

Among the commonly prescribed antibiotics for CAP are macrolides (either alone or in combination with β-lactams), fluoroquinolones, and a combination of third-generation cephalosporins with macrolides.[42] An anionic fluoroquinolone, delafloxacin, has been recently approved for difficult-to-treat patients. It was shown to be superior to moxifloxacin especially when comorbidities like asthma or COPD are present.[42] According to the American Thoracic Society, Infectious Diseases Society of America, and Canadian Guidelines, the initial empiric treatment for CAP is either macrolides, fluoroquinolones, or doxycycline (Vibramycin) if outpatient or intravenous beta-lactams in combination with a macrolide or fluoroquinolones alone if inpatient.[43]

This study alerted the Specialty Hospital to uncover and work on the area of improvement to enhance adherence to the clinical guidelines and the Antibiotic Stewardship Program across the isolation floors. This study will enable the Specialty Hospital to enhance the implementation of the best practices to serve as a model for other hospitals in Jordan, as it will dramatically optimize patient clinical outcomes, and reduce the trend of antibiotic resistance aligned with a reduction in the healthcare costs.

Strengths and limitations of the study

The study is novel in these aspects: First, this study is classified as the first conducted study in Jordan that highlighted the best practice among healthcare providers in regards to prescribing and dispensing antibiotics to hospitalized admitted patients diagnosed with CAP. Second, it is the first study that measures the adherence level of the Antibiotic Stewardship Program in Jordan. Third, a unique electronic technology system is used for data collection to minimize confounders and bias. However, the sample size was selected from only one hospital in Jordan, so the discovered practice cannot be generalized among all Jordanian hospitals. Moreover, as this is a retrospective study, it could be prone to confounding (other risk factors were present but not measured) or recall bias when collecting the data. There is also limited diversity among the population sample.

CONCLUSION

This study covered a high adherence level (80.0%) to CAP clinical guidelines applied to ICU patients in Jordan. On the other hand, around 64 (98.5%) out of the total patients who had treatment regimens on the isolation floors, were noncompliant with clinical guidelines, and such practice led to a negative impact on the clinical output for these patients as the total planned duration of antibiotics was increased compared with

that of patients in the adherent group. This study defined the relationship between significant and nonsignificant variables with adherence level to the Specialty Hospital CAP clinical guidelines, which include: the initial antibiotic regimen, the 72 hours' reassessment, whether antibiotics were switched after culture results were available, primary diagnosis, the total planned duration of antibiotic and choice of antibiotic therapy. This study highlights the need for strict hospital control policies to adhere to guidelines on the isolation floors and lower the burden on hospital services.

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References

1. Adler N, Weber H, Gunadasa I, et al. Adherence to therapeutic guidelines for patients with community-acquired pneumonia in Australian hospitals. Clin Med Insights Circ Respir Pulm Med. 2014;8:17-20. https://doi.org/10.4137/CCRPM.S17978
2. Brown PD. Adherence to guidelines for community-acquired pneumonia: does it decrease cost of care? Pharmacoeconomics. 2004;22(7):413-433. https://doi.org/10.2165/00019053-200422070-00001
3. Triantafyllidis C, Kapordelis V, Papaetis GS, et al. Guidelines adherence for patients with community acquired pneumonia in a Greek hospital. Eur Rev Med Pharmacol Sci. 2012;16(1):1-9.
4. Kolditz M, Ewig S. Community-Acquired Pneumonia in Adults. Dtsch Arztebl Int. 2017;114(49):838-848. https://doi.org/10.3238/arztebl
5. Watkins RR, Lemonovich TL. Diagnosis and management of community-acquired pneumonia in adults. Am Fam Physician. 2011;83(11):1299-1306.
6. Christensen D, Luna CM, Martínez J, et al. Cumplimiento con las guías nacionales en pacientes hospitalizados con neumonía adquirida en la comunidad. Resultados del estudio CAPO en Argentina [Adherence with national guidelines in hospitalized patients with community-acquired pneumonia. Results of CAPO study in Argentina]. Medicina (B Aires). 2007;67(6 Pt 2):709-722.
7. Levy G, Perez M, Rodríguez B, et al. Adherence with national guidelines in hospitalized patients with community-acquired pneumonia: results from the CAPO study in Venezuela. Arch Bronconeumol. 2015;51(4):163-168. https://doi.org/10.1016/j.arbres
8. Corrêa Rde A, Lundgren FL, Pereira-Silva JL, et al. Comissão de Infecções Respiratórias e Micoses - Sociedade Brasileira de Pneumologia e Tisiologia. Brazilian guidelines for community-acquired pneumonia in immunocompetent adults - 2009. J Bras Pneumol. 2009;35(6):574-601. https://doi.org/10.1590/s1806-37132009000600011
9. Feldman C, Anderson R. Community-Acquired Pneumonia: Pathogenesis of Acute Cardiac Events and Potential Adjunctive Therapies. Chest. 2015;148(2):523-532. https://doi.org/10.1378/chest.15-0484
10. Ferreira HLDS, Costa KLP, Cariolano MS, et al. High incidence of rhinovirus infection in children with community-acquired pneumonia from a city in the Brazilian pre-Amazon region. J Med Virol. 2019;91(10):1751-1758. https://doi.org/10.1002/jmv.25524
11. Lanks CW, Musani AI, Hsia DW. Community-acquired Pneumonia and Hospital-acquired Pneumonia. Med Clin North Am. 2019;103(3):487-501. https://doi.org/10.1016/j.mcna.2018.12.008
12. Mantero M, Tarsia P, Gramegna A, et al. Antibiotic therapy, supportive treatment and management of immunomodulation-inflammation response in community acquired pneumonia: review of recommendations. Multidiscip Respir Med. 2017;5(12):26. https://doi.org/10.1186/s40248-017-0106-3
13. Schnoor M, Hedicke J, Dalhoff K, et al. Approaches to estimate the population-based incidence of community acquired pneumonia. J Infect. 2007;55(3):233-242. https://doi.org/10.1016/j.jinf.2007.04.355
14. Thomas CP, Ryan M, Chapman JD, et al. Incidence and cost of pneumonia in medicare beneficiaries. Chest. 2012;142(4):973-981. https://doi.org/10.1378/chest.11-1160
15. Micek ST, Kollef KE, Reichley RM, et al. Health care-associated pneumonia and community-acquired pneumonia: a single-center experience. Antimicrob Agents Chemother. 2007;51(10):3568-3640. https://doi.org/10.1128/AAC.00851-07
16. Ramirez JA, Anzueto AR. Changing needs of community-acquired pneumonia. Journal of Antimicrobial Chemotherapy. 2011;66(3):3-9. https://doi.org/10.1093/jac/dkr094
17. Rozenbaum MH, Pechlivanoglou P, van der Werf TS, et al. The role of Streptococcus pneumoniae in community-acquired pneumonia among adults in Europe: a meta-analysis. Eur J Clin Microbiol Infect Dis. 2013;32(3):305-321. https://doi.org/10.1007/s10096-012-1778-4
18. von Baum H, Schweiger B, Welte T, et al. How deadly is seasonal influenza-associated pneumonia? The German Competence Network for Community-Acquired Pneumonia. Eur Respir J. 2011;37(5):1151-7. https://doi.org/10.1183/09031936.00037410
19. Wunderink RG, Waterer G. Advances in the causes and management of community acquired pneumonia in adults. BMJ. 2017;358-372. https://doi.org/10.1136/bmj.j2471

20. Bosso JA, Drew RH. Application of antimicrobial stewardship to optimise management of community acquired pneumonia. International Journal of Clinical Practice. 2011;65(7):775-783. https://doi.org/10.1111/j.1742-1241.2011.02704.x

21. Silveira CD, Ferreira CS, Corrêa Rde A. Adherence to guidelines and its impact on outcomes in patients hospitalized with community-acquired pneumonia at a university hospital. J Bras Pneumol. 2012;38(2):148-207. https://doi.org/10.1590/s1806-37132012000200002

22. Blasi F, Garau J, Medina J, et al. Current management of patients hospitalized with community-acquired pneumonia across Europe: outcomes from REACH. Respir Res. 2013;14(1):44. https://doi.org/10.1186/1465-9921-14-44

23. Bantar C, Bavestrello L, Curcio D, et al. Acute community-acquired pneumonia in adults: guidelines for initial antimicrobial therapy based on local evidence from a South American Working Group (ConsenSur). J Chemother. 2002;14 (Suppl 4):1-22. https://doi.org/10.1080/1120009x.2002.11782352

24. Ewig S, Birkner N, Strauss R, et al. New perspectives on community-acquired pneumonia in 388 406 patients. Results from a nationwide mandatory performance measurement programme in healthcare quality. Thorax. 2009;64(12):1062-1071. https://doi.org/10.1136/thx.2008.109785

25. Lim TK, Chew MY. Management of severe community acquired pneumonia in the emergency department. Journal of Emergency and Critical Care Medicine. 2018;2(2):2-4. https://doi.org/10.21037/jeccm.2017.12.12

26. Lim WS, Baudouin SV, George RC, et al. Pneumonia Guidelines Committee of the BTS Standards of Care Committee. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax. 2009;64(Suppl 3):1-55. https://doi.org/10.1136/thx.2009.121434

27. Lutfiyya MN, Henley E, Chang LF, et al. Diagnosis and treatment of community-acquired pneumonia. Am Fam Physician. 2006;73(3):442-450.

28. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America, American Thoracic Society. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44(Suppl 2):S27-72. https://doi.org/10.1086/511159

29. Prina E, Ranzani OT, Torres A. Community-acquired pneumonia. Lancet. 2015;386(9998):1097-1108. https://doi.org/10.1016/S0140-6736(15)60733-4

30. Quan TP, Fawcett NJ, Wrightson JM, et al. Increasing burden of community-acquired pneumonia leading to hospitalisation, 1998-2014. Thorax. 2016;71(6):535-542. https://doi.org/10.1136/thoraxjnl-2015-207688

31. Torres A, Sibila O, Ferrer M, et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: a randomized clinical trial. JAMA. 2015;313(7):677-750. https://doi.org/10.1001/jama.2015.88

32. Tschernig T. Hospital-acquired pneumonia and community-acquired pneumonia: two guys? Annals of Translational Medicine. 2016;4(S1):S22. https://doi.org/10.21037/atm.2016.10.10

33. Yu H, Rubin J, Dunning S, et al. Clinical and economic burden of community-acquired pneumonia in the Medicare fee-for-service population. J Am Geriatr Soc. 2012;60(11):2137-2180. https://doi.org/10.1111/j.1532-5415.2012.04208

34. Chalmers J, Campling J, Ellsbury G, et al. Community-acquired pneumonia in the United Kingdom: a call to action. Pneumonia (Nathan). 2017;5(9):15. https://doi.org/10.1186/s41479-017-0039-9

35. Bosso JA, Drew RH. Application of antimicrobial stewardship to optimize management of community-acquired pneumonia. Int J Clin Pract. 2011;65(7):775-851. https://doi.org/10.1111/j.1742-1241.2011.02704.x

36. Sharma R, Sandrock CE, Meehan J, et al. Community-Acquired Bacterial Pneumonia—Changing Epidemiology, Resistance Patterns, and Newer Antibiotics: Spotlight on Delafloxacin. Clin Drug Investig. 2020;40(10):947-960. https://doi.org/10.1007/s40261-020-00953-z

37. Brown JS. Community-acquired pneumonia. Clin Med (Lond). 2012;12(6):538-543. https://doi.org/10.7861/clinmedicine.12-6-538

38. Foolad F, Huang AM, Nguyen CT. A multicentre stewardship initiative to decrease excessive duration of antibiotic therapy for the treatment of community-acquired pneumonia. J Antimicrob Chemother. 2018;73(5):1402-1407. https://doi.org/10.1093/jac/dky021

39. Kurtzhalts KE, Sellick JA Jr, Ruh CA, et al. Impact of Antimicrobial Stewardship on Outcomes in Hospitalized Veterans with Pneumonia. Clin Ther. 2016;38(7):1750-1758. https://doi.org/10.1016/j.clinthera.2016.06.004

40. Grenier C, Pépin J, Nault V. Impact of guideline-consistent therapy on outcome of patients with healthcare-associated and community-acquired pneumonia. J Antimicrob Chemother. 2011;66(7):1617-1624. https://doi.org/10.1093/jac/dkr176

41. Fésüs A, Benkő R, Matuz M, et al. Impact of Guideline Adherence on Outcomes in Patients Hospitalized with Community-Acquired Pneumonia (CAP) in Hungary: A Retrospective Observational Study. Antibiotics. 2022;11(4):468. https://doi.org/10.3390/antibiotics11040468

42. Sharma R, Sandrock CE, Meehan J, et al. Community-Acquired Bacterial Pneumonia-Changing Epidemiology, Resistance Patterns, and Newer Antibiotics: Spotlight on Delafloxacin [published correction appears in Clin Drug Investig. 2021 Feb;41(2):197]. Clin Drug Investig. 2020;40(10):947-960. https://doi.org/10.1007/s40261-020-00953-z

43. Lutfiyya MN, Henley E, Chang LF, et al. Diagnosis and treatment of community-acquired pneumonia. Am Fam Physician. 2006;73(3):442-450.