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## Empiric Antibiotic Therapy in the Treatment of Community-acquired Pneumonia in a General Hospital in Saudi Arabia

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### Abstract

#### Background:

Guideline-based empiric antimicrobial therapy is recommended for the treatment of community-acquired pneumonia (CAP). In this study, we evaluate the pattern of empiric antibiotics of CAP patients.

#### Materials and Methods:

Patients with CAP were retrieved from the health information unit using the International Classification of Diseases, Ninth Revision. The electronic pharmacy database was used to retrieve prescribed antibiotics and the duration of therapy for each antibiotic.

#### Results:

A total of 1672 adult patients were included in the study and 868 (52%) were male. Of all the patients, 47 (2.8%) were admitted to the intensive care unit (ICU). The most frequently used antibiotics were levofloxacin (68.12%), ceftriaxone (37.7%), imipenem-cilastatin (32.5%), and azithromycin (20.6%). The mean days of therapy of each of these antibiotics were 3.2, 2.8, 4.4, and 2.9, respectively. A combination therapy of levofloxacin and imipenem-cilastatin was prescribed for 355 (21.8%) of non-ICU patients versus 20 (60.6%) of ICU patients ( $P = 0.0007$ ). Imipenem-cilastatin was prescribed for 518 (31.8%) of non-ICU

patients versus 25 (56.8%) of ICU patients ( $P = 0.0009$ ). Levofloxacin was prescribed for 1106 (68%) of non-ICU patients versus 33 (75%) of ICU patients ( $P = 0.412$ ). Ceftriaxone use decreased significantly from 40.9% in 2013 to 25.9% in 2016 ( $P = 0.034$ ). In addition, levofloxacin use increased from 63.7% to 75% ( $P = 0.63$ ).

### Conclusion:

The most commonly used antibiotics were levofloxacin, ceftriaxone, imipenem-cilastatin, and azithromycin. The data call for further refinement and prospective audit of antibiotic use in CAP, especially in non-ICU settings.

**Keywords:** Antimicrobial stewardship, antimicrobial therapy, community-acquired pneumonia, empiric antibiotic

### INTRODUCTION

Community-acquired pneumonia (CAP) is an important admission diagnosis with an annual admission of 664 patients in our hospital,[1] with an annual rate of 44/1000 patients. Guideline-based empiric antimicrobial therapy is recommended for the treatment of CAP by the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA).[2] Few studies examined different aspects of CAP in Saudi Arabia.[3,4,5,6] Limited data regarding the adherence to ATS/IDSA guidelines are available from this part of the world. One study included patients from the United Arab Emirates, Kuwait, Bahrain, Oman, and Qatar[7] and one study from Oman only[8] evaluated the adherence to the Gulf Cooperation Council (GCC) CAP guidelines.[4] In this study, we evaluate the rate of CAP patients who received the recommended antibiotics based on local and international guidelines.[2,4] In addition, we evaluate the trend over time of the use different antibiotics and the use of combination therapy.

### MATERIALS AND METHODS

This is a retrospective chart review of adults with CAP who were admitted to a general hospital in Saudi Arabia from March 2013 to June 2016. The hospital is a 350-bed general hospital and provides medical care for 160,000 individuals eligible for medical care.[9] The patients' data were retrieved from the health information unit using the International Classification of Diseases, Ninth Revision (ICD-9). The electronic pharmacy database was then used to retrieve the prescribed antibiotics and the duration of therapy for each antibiotic. A standard Microsoft Excel sheet was used to record the retrieved data. Statistical analysis was done using Minitab®(Minitab Inc. Version 17, State College, Pennsylvania, USA; 2017). The generated data included the mean duration of each antibiotic standard deviation ( $\pm$ SD). A significant  $P$  value was considered if  $P < 0.05$ . The study was approved by the JHAH Institutional Review Board. The diagnosis of CAP was based on the presence of a group of clinical features such as fever and the demonstration of an infiltrate by chest radiograph with or without supporting microbiological data as suggested by the ATS/IDSA.[2] We also calculated the CURB-65 score based on Confusion, Blood Urea, Respiratory Rate, Blood pressure, and age  $\geq 65$  years.

### RESULTS

A total of 1672 adult patients were admitted during the study period. Of those patients, 868 (52%) were male. Of all patients, 47 (2.8%) were admitted initially to the intensive care unit (ICU). The mean CURB-65 score (confusion, blood urea, respiratory rate, blood pressure, and age  $> 65$  years) ( $\pm$ SD) was 1.47 (1.15)

and 1.8 (0.92) for patients who did not require ICU and those who required ICU admission ( $P = 0.019$ ). The most frequently used antibiotics as single agents or combined with other antibiotics were levofloxacin (68.12%); ceftriaxone (37.7%), imipenem-cilastatin (32.5%), and azithromycin (20.6%). The mean days of the use of these antibiotics were 3.2, 2.8, 4.4, and 2.9, respectively [Figure 1]. The overall mean ( $\pm$ SD) days of therapy of antibiotics was 5.96 ( $\pm$ 4.8) and a median of 5 days [Figure 2].

A combination therapy of levofloxacin and imipenem-cilastatin was prescribed for 355 (21.8%) of non-ICU patients versus 20 (60.6%) of ICU patients ( $P = 0.0007$ ). Levofloxacin was prescribed for 1106 (68%) of non-ICU patients versus 33 (75%) of ICU patients ( $P = 0.412$ ). Imipenem-cilastatin was prescribed for 518 (31.8%) of non-ICU patients versus 25 (56.8%) of ICU patients ( $P = 0.0009$ ). There was no relationship between antibiotic use and the CURB-65 score [Figure 3].

There was no time-trend difference in the percentage of patients receiving imipenem-cilastatin (34.6%) and azithromycin (21.7%–18.3%) [Figure 4]. However, ceftriaxone use decreased from 41% in 2013 to 26% in 2016 ( $P = 0.034$ ). In addition, levofloxacin use increased from 63.7% to 75% ( $P = 0.63$ ).

## DISCUSSION

This is the largest study from the Gulf region to investigate antimicrobial therapy of admitted CAP patients. Two previous smaller studies addressed this issue and one of them was a multicenter.[7,8] The current study showed that combination therapy of levofloxacin and imipenem-cilastatin was prescribed for 21.8% of non-ICU patients compared to 60.6% of ICU patients and that imipenem-cilastatin was prescribed for 31.8% of non-ICU patients compared to 56.8% of ICU patients. The overall empiric antibiotic use in CAP in the current study was in alignment with those of the ATS/IDSA.[2] Various studies showed that the overall guideline adherence rate for empiric antibiotic therapy for CAP was 31.2%–48%.[10,11,12] The compliance rate of empiric antibiotic use in CAP was very low (6.4%) in one study from Europe in 2006[13] and was 66% in a study from South Africa.[14] Adherence to CAP guidelines was associated with better prognosis in the short term, especially in patients requiring mechanical ventilation.[15] The rate of initial ICU admission of CAP patients was low (2.8%) in the present study. This rate is comparable to the rate from Hong Kong (4%) and lower than rates from Spain (17%) and United Kingdom (8.7%).[16,17] However, rates of ICU admission and criteria leading to such admissions may be different among multiple healthcare systems.[18] One study showed that the most common antibiotics used were levofloxacin, amoxicillin-clavulanic acid, and clarithromycin.[13] In a study from China, levofloxacin was the most common initial antibiotic (15.7%).[19] In one study, non-ICU patients received a respiratory fluoroquinolone alone 33% of the time or beta-lactam plus macrolide (19%).[20] In an Australian study, ceftriaxone and azithromycin combination was used for 56% of the patients[21] and one-third of patients with CAP in an Indian study received macrolide and a beta-lactam.[22]

In the current study, imipenem-cilastatin was prescribed for about one-third of non-ICU patients and for over half of ICU patients ( $P = 0.0009$ ). The data suggest that there is room to improve empiric antibiotic usage in non-ICU settings. In an Australian study, many mild CAP patients were treated as a severe CAP with an odds ratio of 8 for mild CAP versus severe CAP.[21] Moreover, in an audit from Britain, initial antibiotics matched local CAP guidelines in only 55.5% of patients.[23] In addition, in one study from the GCC countries, 20.3% of 684 patients were treated with two agents and levofloxacin was the most frequently used (65.7%), followed by ceftriaxone (16.1%) and moxifloxacin (13.1%).[7] Thus, despite the existence of guidelines, the optimal use of antibiotics had not been achieved in CAP. Prospective audit and feedback for the use of antibiotics are still a priority to improve antibiotic stewardship.

In the United States, it was observed that the use of macrolides increased from 20% in 1993 to 30% in 2006 ( $P < 0.001$ ) and an increase in quinolones from 0% to 39% from 1993 through 2008 ( $P < 0.001$ ).<sup>[24]</sup> We found no change in the prescribing pattern of azithromycin and imipenem-cilastatin, and there was a significant decrease in ceftriaxone paralleled by an increase in levofloxacin use. Previous studies from Saudi Arabia did not address the rate of *Streptococcus pneumoniae* resistance to quinolone<sup>[25,26]</sup> or showed a very low resistance rate.<sup>[27]</sup> Thus, further studies are needed to examine the change in *S. pneumoniae* resistance to quinolones in this part of the world. Antibiotic duration and adherence to CAP guidelines are important elements in antibiotic stewardship.<sup>[28]</sup> According to the IDSA guidelines, a minimum of 5 days is needed to treat patients with CAP.<sup>[2]</sup> The mean duration of therapy of each antibiotic was 2.8–4.4 days, with mean antibiotic days of  $7 \pm 5$  days.

This study has limitations and includes retrospective nature, a single-center study, and the lack of microbiological data. In addition, we depended on ICD coding and did not check the CAP diagnosis using the medical charts. Thus, this is an additional limitation of the study since a misclassified CAP diagnosis may explain some of the noncompliance to guidelines. It is known that there is a wide gap in guideline recommendations and actual usage pattern of antibiotics. Moreover, that this study looked at the gap in practice and compared the data to other parts of the world to highlight any discrepancies to rectify and improve the adherence to antibiotics as per the guidelines for CAP.

## CONCLUSION

There is a room for further antibiotic stewardship in the area of CAP and further refine and prospective audit of antibiotic use in CAP, especially in non-ICU settings.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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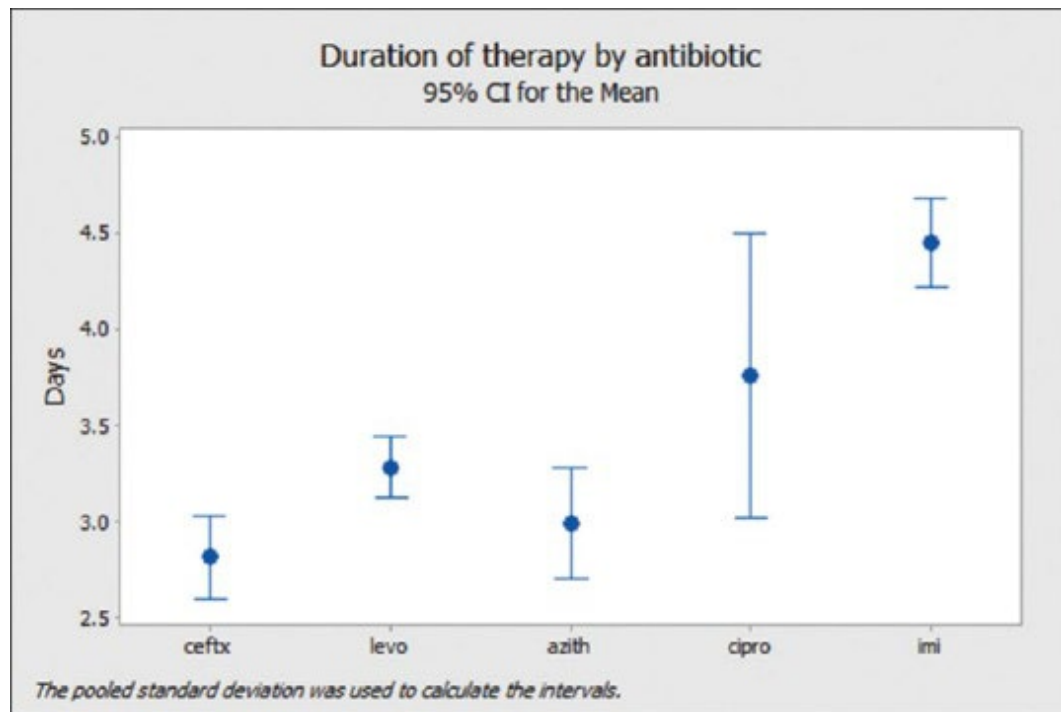
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## Figures and Tables

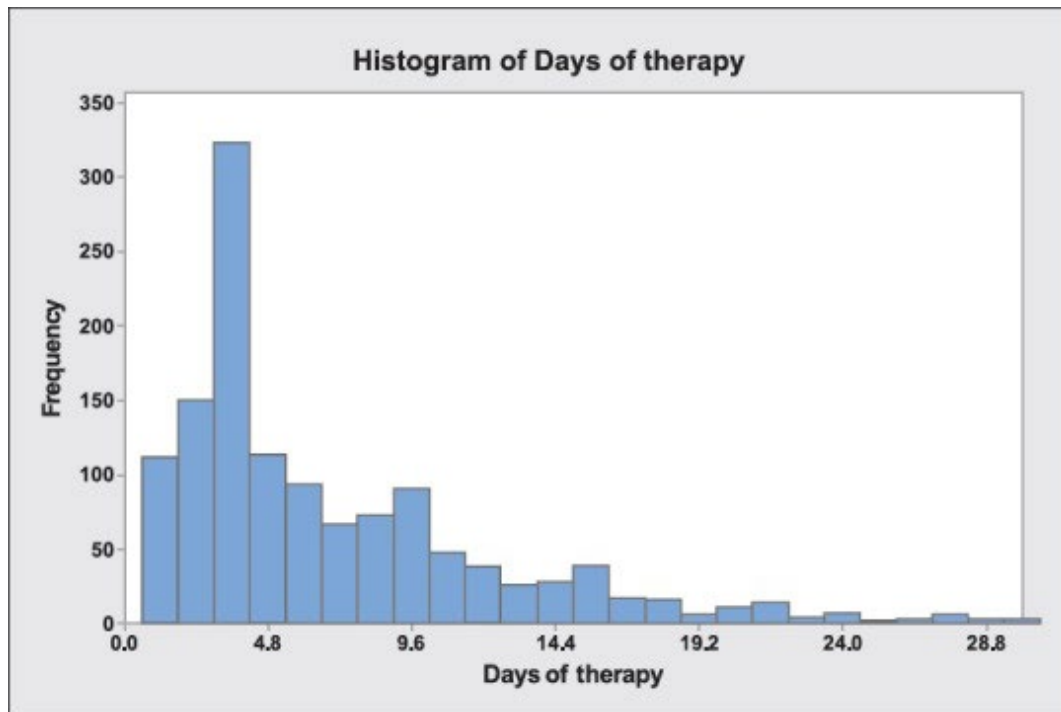
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### Figure 1



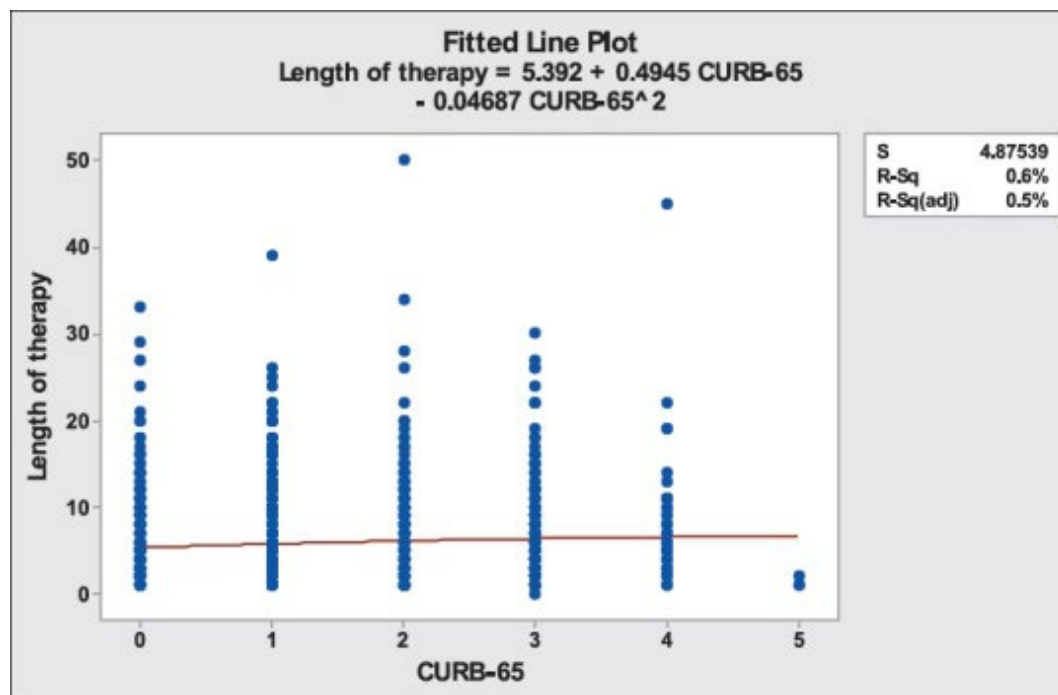
Box blot of the mean and the 95% confidence interval of the duration of commonly used antibiotics (the number of cases in each antibiotic is as follows: Ceftriaxone (ceftx, 631); levofloxacin (levo, 1139); azithromycin (azith, 344); ciprofloxacin (cipro, 54); imipenem (imi, 543)

**Figure 2**



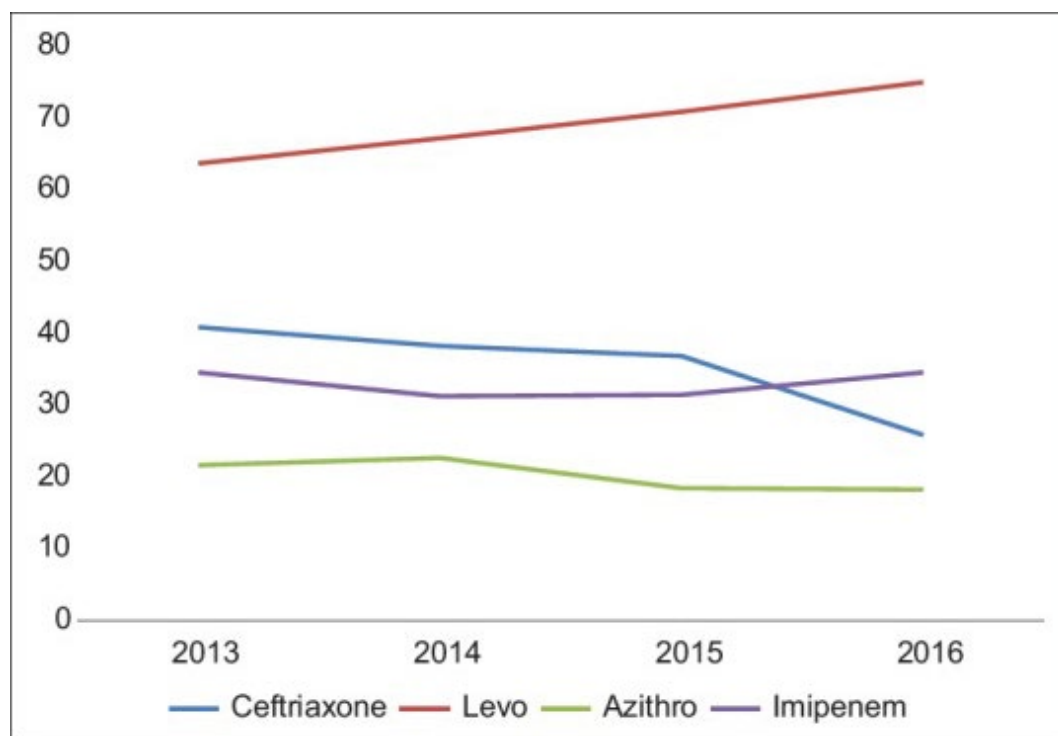
A histogram showing the days of therapy of antibiotics of the included patients

**Figure 3**



A fitted line blot of the length of antimicrobial therapy and the CURB-65 score

**Figure 4**



Percentage of patients receiving specified antibiotics per year of admission

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