Original Article

Evaluation of the Frequency of Antibiotic Stewardship for the Treatment of Pneumonia in a Tertiary Hospital (Loghman Hakim Hospital) in 2021

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Abstract

Background: Pneumonia is one of the common infectious diseases in the community and hospital, which can cause complications and death if not treated. Correct treatment of this disease is important. Therefore, in this study, we aimed to evaluate antibiotic stewardship for pneumonia with the American Thoracic Society (ATS) guidelines in Loghman Hakim Hospital in 2021.

Materials and Methods: In this descriptive study, all patients admitted to Loghman Hakim Hospital in 2021 with pneumonia were evaluated. Age, gender, type of pneumonia (healthcare-associated pneumonia, community-acquired pneumonia, community-acquired aspiration pneumonia, early-onset and late-onset hospital-acquired pneumonia, ventilator-associated pneumonia, and hospital-acquired aspiration pneumonia), antibiotic type and dose, and renal dose adjustment of antibiotics were recorded. Then, the antibiotic prescription protocol in patients with pneumonia was compared with the ATS guidelines.

Results: 72 people were included in the study; 11 (15.28%) had healthcare-associated pneumonia (HCAP), 24(33.33%) community-acquired pneumonia (CAP), 20(27.78%) community-acquired aspiration pneumonia (CAAP), 7(9.72%) hospital-acquired pneumonia (HAP), 4(5.56%) hospital-acquired aspiration pneumonia (HAAP), and 6 (8.33%) patients had ventilator-associated pneumonia (VAP). 31.94% did not receive antibiotics according to the protocol. 13.88% of patients received antibiotics correctly, but with the wrong dose, and in 18.06% of patients, the type of antibiotic was wrong (P-value=0.102).

Conclusion: Monitoring antibiotic stewardship in the hospital for patients with pneumonia is necessary.

Keywords: Antimicrobial stewardship, Community-acquired pneumonia, Healthcare-associated pneumonia, Pneumonia

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Introduction

Antibiotic resistance is spreading in the world; however, the development of antibiotics is progressing slowly[1]. Now and more than ever, preventing unnecessary antibiotic prescriptions is crucial[2]. In other words, the evaluation and improvement of the antibiotic prescription situation by specialists based on the patients' needs (under antibiotic stewardship) will not only be associated with the

reduction and correct management of antibiotic resistance. However, they will also significantly reduce patients' vulnerability level[3-5]. However, the correct and timely selection of antibiotics based on drug sensitivity and resistance is challenging[6].

In 2007, a comprehensive guideline regarding the antibiotic treatment of various types of pneumonia was presented by the American Thoracic Society (ATS). Based on the relevant guidelines, the criteria for antibiotic selection in pneumonia, including etiology and determination of drug resistance, have been established[7]. For example, in the case of pneumonia in patients hospitalized in intensive care units, administering respiratory fluoroquinolones or a combination of beta-lactam and macrolide was introduced as the first effective treatment for pneumonia[7]. In patients admitted to the intensive care unit, the treatment of pneumonia associated with Pseudomonas or methicillin-resistant staphylococcus aureus is suggested[7]. Recently, the use of broad-spectrum antibiotics for different types of pneumonia is not recommended[8,9].

The term "medication errors" can be defined as "making decisions that unintentionally and significantly reduce the effectiveness of treatment or increase the risk of harm compared to practices outlined in standard treatment guidelines"[10]. Non-adherence to national and international guidelines and the unavailability of national prescription methods for patients can be possible reasons for these errors[11]. Prescription errors are common in patients with pneumonia due to the need for dose adjustment, variability between patients, and differences in the pharmacokinetic properties of drugs[12]. One study showed 3 to 20% errors in prescriptions in hospitalized pediatrics[13]. Among all errors, dosage errors are the most common medication errors[14]. Gaining insight into antibiotic prescribing practices and related errors among patients with pneumonia is important to improve current policies and prevent adverse effects. Therefore, this study aimed to evaluate the frequency of antibiotic stewardship for treating pneumonia with ATS guidelines in Loghman Hakim Hospital in 2021.

Methods

In this cross-sectional descriptive study, all pneumonia patients admitted to Loghman Hakim Hospital (Tehran, the capital of Iran) in 2021 were evaluated for antibiotic stewardship.

Inclusion criteria were involvement with pneumonia and hospitalization in the general intensive care unit (ICU), neurosurgery ICU, internal medicine units, cardiac and lung units, and age more than 18 years. Exclusion criteria were involvement with severe sepsis, heart failure, pulmonary thromboembolism, other nosocomial infections, and acute respiratory disease syndrome (ARDS).

The sampling method was sequential non-probability. Based on the study of van de Garde et al[15], the percentage of matching with the optimal antibiotic prescription was 75%. Assuming a confidence level of 0.05 and an accuracy limit of 0.1, the minimum number of samples was 72 patients.

Based on the inclusion and exclusion criteria and the calculated sample size, 72 patients were selected from the above patients and enrolled in the study. After obtaining the necessary permits, patients in cardiopulmonary, internal medicine, general ICU, and neurosurgery ICU departments were assessed for antibiotic stewardship (attached tables). The files of patients diagnosed with pneumonia were selected based on the decision of infectious specialists and radiologists who had the conditions to enter the study and consented to participate. The assessed antibiotic in this study was the antibiotic received as an empirical antibiotic prescribed by the relevant service, and the patient received it during hospitalization.

The patients' files were reviewed to complete the information including sex, age, type of pneumonia (healthcare-associated pneumonia (HCAP), community-acquired pneumonia (CAP), community-acquired aspiration pneumonia (CAAP), early and late hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), and hospital-acquired aspiration pneumonia (HAAP)), type of antibiotic, dose of antibiotic, and dose adjustment of antibiotic was done. Then, by noting the antibiotic orders were compared to the ATS guidelines 2019[16] as standard protocol.

In this study, any deviation from the mentioned instructions regarding the type and dose of antibiotic and the need to adjust the renal dose was considered a "mismatch".

Mean and standard deviations were used to describe quantitative data and frequency and percentages were used for qualitative data. The chi-square test was used to compare qualitative variables between groups, and Fisher's exact test was used to compare the mean of quantitative variables using the ANOVA test. All analyses were performed using SPSS 25.0 statistical software. A P-value less than 0.05 was considered statistically significant.

The ethical principles of the research were respected, and the information of all patients remained confidential. This research received the ethical code from the ethics committee of Shahid Beheshti Medical University (IR.SBMU.MSP.REC.1400.268).

Results

The data of 72 patients with pneumonia admitted to Loghman Hakim Hospital in 2021 were collected and analyzed. Of all patients, 11 (15.28%) had HCAP, 24 (33.33%) CAP, 20 (27.78%) CAAP, 7 (9.72%) HAP, 4 (5.56%) HAAP, and finally 6 (8.33%) had VAP. Of all patients, 47 (65.28%) were male and 25 (34.72%) were female. The distribution of patients based on the wards that were admitted is seen in **figure 1**.

In **Table 1**, the patients' demographics, medications, and ward-related data are specified according to the type of pneumonia.

The mean age of the patients in the VAP group was 48 ± 14.23 years, and the highest age group was in the HCAP group (75.73 ± 16.62 years), which was clinically significant (P-value=0.021). The gender distribution of patients was the same between the groups (P-value=0.561). This means there was no statistically significant relationship between the gender of patients and the type of pneumonia. The type of hospitalization ward was also evaluated, which showed that HCAP, CAP, and CAAP were mostly hospitalized in the heart and lung ward (P-value=0.009).

Regarding matching the types of antibiotics with the ATS guideline, 49 (68.1%) patients received the correct antibiotic based on the guideline, and 23 (31.9%) patients received incorrect or different antibiotics based on the guideline. A total of 31.9% of antibiotic prescriptions had mismatches based on the guideline. These data and

In **Table 2**, the dosage of antibiotics between the two groups with and without antibiotic mismatch was evaluated. As can be seen, of 72 patients, 62 patients had renal dose matching, and ten patients had renal dose mismatch. Out of the ten patients, one in the HCAP group, 4 in the CAP, 2 in the CAAP, 2 in the HAP, 1 in the HAAP, and zero in the VAP group had renal dose mismatch. Significantly, patients with the agreement of antibiotic prescription also had kidney dose adjustment. Significantly, patients with antibiotic matching also had kidney dose adjustment (P-value=0.001).

In **Table 3**, we evaluated the relationship between the distribution of patients based on antibiotic matching with the guideline and clinical and demographic data.

In total, in 31.94% of cases, antibiotic mismatch was seen. In 13.88% of cases, the wrong dose of antibiotic

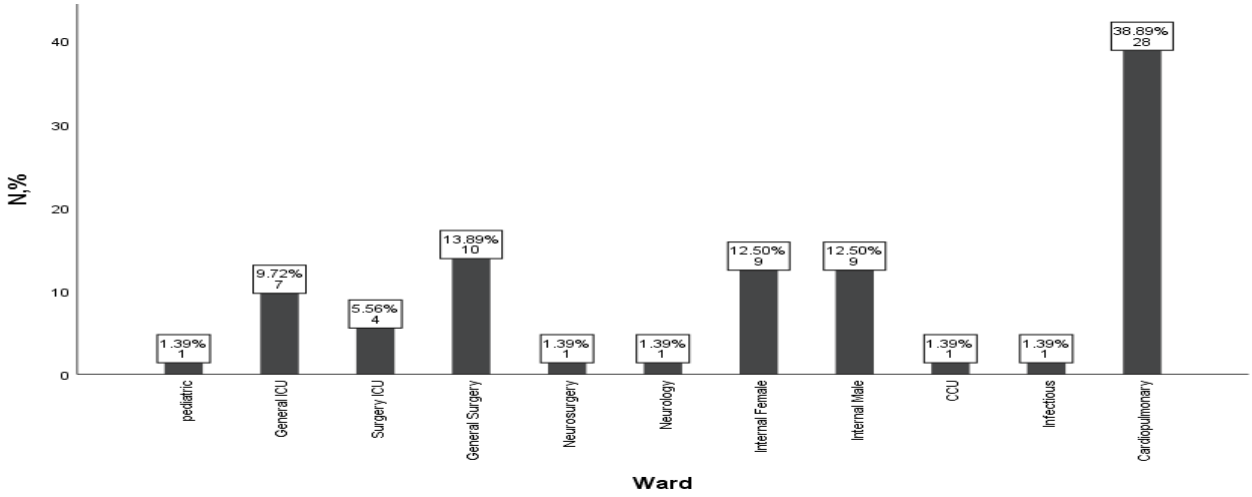

Figure 1. The distribution of patients based on the type of ward.

Table 1: The demographic, medication, and hospitalization ward data based on the type of pneumonia.

		Groups					
		HCAP	**CAP**	**HAP**	**HAAP**	**VAP**	**P-value**
Age		75.73 ± 16.62	72.63 ± 16.8	65.57 ± 26.12	75 ± 8.6	48 ± 14.23	0.021*
Sex	Male	9 (81.8%)	14 (58.3%)	5 (71.4%)	3 (75.0%)	5 (83.3%)	0.561**
	Female	2 (18.2%)	10 (41.7%)	2 (28.6%)	1 (25.0%)	1 (16.7%)	--
Weight		76.6 ± 5.18	73.22 ± 8.36	71.5 ± 2.12	65 ± 0	76.4 ± 15.04	0.417*
Hospitalized duration		17.82 ± 16.79	8.21 ± 10.05	26.57 ± 20	11.75 ± 11.27	24 ± 7.07	0.004*
Prognosis	Alive	6 (54.5%)	18 (75.0%)	4 (57.1%)	0 (0.0%)	1 (16.7%)	0.024**
	Expire	5 (45.5%)	6 (25.0%)	3 (42.9%)	4 (100.0%)	5 (83.3%)	--
Wards	Pediatric	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0.003**
	General ICU	0 (0.0%)	1 (4.2%)	3 (42.9%)	0 (0.0%)	1 (16.7%)	--
	Surgery ICU	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (50.0%)	--
	General Surgery	0 (0.0%)	2 (8.3%)	1 (14.3%)	2 (50.0%)	2 (33.3%)	--
	Neurosurgery	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	--
	Neurology	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	--
	Internal Female	2 (18.2%)	3 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	--
	Internal Male	2 (18.2%)	3 (12.5%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	--
	CCU	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	--
	Infectious	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	--
	Cardiopulmonary	6 (54.5%)	13 (54.2%)	1 (14.3%)	1 (25.0%)	0 (0.0%)	--
Creatinine		1.72 ± 2.01	1.27 ± 0.52	1.09 ± 0.37	1.7 ± 0.68	1.3 ± 0.85	0.714*

*P-value based on ANOVA, **P-value based on Chi-square and Fisher exact test

Table 3: Relationship between antibiotic matching and clinical and demographic data.

		AB matching		
		False	**True**	**P-value**
Gender	Male	11 (47.8%)	36 (73.5%)	0.06**
	Female	12 (52.2%)	13 (26.5%)	-
Type of pneumonia	HCAP	4 (17.4%)	7 (14.3%)	0.6**
	CAP	8 (34.8%)	16 (32.7%)	-
	CAAP	7 (30.4%)	13 (26.5%)	-
	HAP	2 (8.7%)	5 (10.2%)	-
	HAAP	2 (8.7%)	2 (4.1%)	-
	VAP	0 (0.0%)	6 (12.2%)	-
Ward	Pediatric	0 (0.0%)	1 (2.0%)	0.5**
	General ICU	2 (8.7%)	5 (10.2%)	-
	Surgery ICU	0 (0.0%)	4 (8.2%)	-
	General Surgery	3 (13.0%)	7 (14.3%)	-
	Neurosurgery	0 (0.0%)	1 (2.0%)	-
	Neurology	0 (0.0%)	1 (2.0%)	-
	Internal Female	3 (13.0%)	6 (12.2%)	-
	Internal Male	2 (8.7%)	7 (14.3%)	-
	CCU	1 (4.3%)	0 (0.0%)	-
	Infectious	1 (4.3%)	0 (0.0%)	-
	Cardiopulmonary	11 (47.8%)	17 (34.7%)	-
Age		74.09 ± 15.01	69.49 ± 18.75	0.3*

*P-value based on T-test, **P-value based on Chi-square and Fisher exact test

was prescribed, and in all cases (31.94%), the wrong type of antibiotic was prescribed. 31.94% of patients received the wrong type of antibiotic, and 13.88% received the wrong dose.

Among the patients who had an antibiotic mismatch with the guideline, 52.2% died, and among the patients

Table 2: Prevalence of antibiotic mismatching based on renal dose adjustment.

		Antibiotic matching		
		No (23)	Yes (49)	P-value
Renal dose adjustment	No	10 (34.8%)	0 (4.1%)	**0.001**
	Yes	15 (65.2%)	47 (95.9%)	--
Vancomycin 500		4 (17.4%)	6 (12.2%)	0.7
Vancomycin 1		4 (17.4%)	17 (34.7%)	0.1
Imipenem 1		1 (4.3%)	1 (2.0%)	0.5
Imipenem 500		2 (8.7%)	3 (6.1%)	0.6
Imipenem 250		1 (4.3%)	0 (0.0%)	0.3
Ciprofloxacin 400		4 (17.4%)	8 (16.3%)	>0.9
Ciprofloxacin 200		2 (8.7%)	2 (4.1%)	0.5
Meropenem 2		1 (4.3%)	2 (4.1%)	>0.9
Meropenem 1		2 (8.7%)	15 (30.6%)	0.07
Meropenem 500		0 (0.0%)	2 (4.1%)	>0.9
Tazocin 4.5		4 (17.4%)	3 (6.1%)	0.1
Tazocin 3.375		3 (13.0%)	1 (2.0%)	0.09
Tazocin 2.25		0 (0.0%)	3 (6.1%)	0.5
Amikacin 1		0 (0.0%)	1 (2.0%)	>0.9
Amikacin 750		1 (4.3%)	2 (4.1%)	>0.9
Cefteriaxon 1		10 (43.5%)	12 (24.5%)	0.1
Cefteriaxon 2		1 (4.3%)	0 (0.0%)	0.3
Linezolide 400		0 (0.0%)	1 (2.0%)	>0.9
Linezolide 600		0 (0.0%)	2 (4.1%)	>0.9
Colistin 9		0 (0.0%)	1 (2.0%)	>0.9
Colistin 6.4		0 (0.0%)	1 (2.1%)	>0.9
Colistin 4.5		0 (0.0%)	3 (6.1%)	0.5
Azithromycin 500		2 (8.7%)	0 (0.0%)	0.09
Levofloxacin 750		1 (4.3%)	8 (16.3%)	0.2
Levofloxacin 500		2 (8.7%)	4 (8.2%)	>0.9
Levofloxacin 250		0 (0.0%)	1 (2.1%)	>0.9
Clindamycin 600		5 (21.7%)	4 (8.2%)	0.1
Tavanex 500		0 (0.0%)	1 (2.0%)	>0.9
Cefepim 1		1 (4.3%)	1 (2.0%)	0.5
Cefepim 2		0 (0.0%)	1 (2.0%)	>0.9

**P-value based on Chi-square and Fisher exact test

who had antibiotic matching, 44.9% died. This difference was not statistically significant (P-value=0.619).

Discussion

The current study evaluated the frequency of antibiotic mismatching based on antibiotic stewardship for pneumonia based on ATS guidelines in Loghman Hakim Hospital in 2021. This study evaluated all patients hospitalized in different hospital wards due to non-infectious disorders and were involved with pneumonia (including CAP, CAAP, HCAP, VAP, HAP, and HAAP). Seventy-two patients were evaluated, of which 72 patients, 11(15.28%) had HCAP, 24(33.33%) had CAP, 20 (27.78%) had CAAP, 7 (9.72%) had HAP, 4 (5.56%) had HAAP, and 6 (8.33%) had VAP. In all patients, there was a total antibiotic mismatch of 31.94%. In 13.88% of cases, the wrong dose of antibiotic was prescribed, and in all cases (31.94%), the wrong type of antibiotic was prescribed. 31.94% of patients received the wrong antibiotic, and 13.88% received the wrong dose and the wrong type of antibiotic.

In the current study, it was seen that the lowest mean age of patients was in the VAP group (48±14.23 years), and the highest was in the HCAP (group 75.73±16.62 years), which was a statistically significant difference in the age. In some studies, it has been seen that patients with HCAP were older compared to patients with other types of pneumonia[17-19]. The findings of these studies are in line with the present study. One of the risk factors of HCAP is living in nursing homes[20], which can be the reason for the high age of HCAP patients in this study, which, of course, needs to be investigated in future studies.

In the current study, it was seen that 31.94% of patients did not receive appropriate antibiotics. The appropriateness of the antibiotic was based on the correctness of the type of prescribed antibiotic and also the appropriate dose for the patients of other departments in the form of Stewardship, which was evaluated based on the ATS criteria. It was also seen that among the 31.94% of patients who received the wrong antibiotic, in 13.88% of the cases, the prescribed type and dose of antibiotics were wrong. The study by Hassler et al. showed that during four years in patients with HCAP, 19.6% of antibiotics were matched entirely with the guideline, 21.7% were partially matched, and 58.9% received the wrong or mismatched antibiotics. Mismatching with guidelines increased with

hospitalization time. Rates of fully or partially Mismatched antibiotics varied among US hospitals (median 36.4%). As seen in Hasler et al.'s study, inappropriate antibiotic prescriptions are high in patients with pneumonia[21]. The causes of these mismatched prescribed antibiotics need to be investigated in future studies, but several factors seem to be involved. One of the factors we observed was the lack of coordination between different services. For example, for a patient who was hospitalized in other wards except the infectious department and was involved with pneumonia, an infectious consultation was requested, and after placing medication orders and adjusting the drug dosage by the infectious disease service, the infectious disease department's drug order was either not implemented at all, or the relevant ward's doctors changed the drug dose prescribed by the infectious service. This issue requires a strong monitoring system to implement these hospital protocols strictly.

Another reason that seems important in this condition is the difference between the initial and final diagnoses of pneumonia. For example, a patient may initially appear to have CAP and be treated with a CAP protocol but later be diagnosed with HCAP without changing the patient's antibiotic, as was seen in Hassler et al.'s study[21]. There seems to be a strong need for extensive studies to solve this problem.

One of the advantages of the current study in comparison with Hassler et al.'s study was the investigation of all types of pneumonia in the hospital, but one of the disadvantages was the shorter duration of the study, in the current study, and as its result, the number of patients was less in our study.

Correcting these antibiotic errors, in addition to the need for scientific steps, requires management work because the best and most proficient person to prescribe antibiotics in hospital settings is an infectious disease specialist, and it is necessary that according to the prospective audit and feedback method, in a Friendly atmosphere, different doctors of the patient talk with the infectious disease specialist about the reasons for prescribing the type of antibiotic.

Regarding strategies to reduce antibiotic prescription errors in the hospital, in the study by Faine et al., a pharmacist who checks the drugs makes patients significantly more likely to receive appropriate empirical antimicrobial treatment (58.3% vs. 38.3%). Regardless of pneumonia type, when an emergency medical pharmacist checked the drugs, the patients were significantly more likely to receive appropriate antimicrobial therapy (CAP, 77.7% vs. 52.9% p=0.008; HCAP, 47.7% vs. 28.8%, P=0.005)[22]. It is one of the good solutions for appropriate antibiotic prescriptions in the hospital. Every hospital needs the presence of active and skilled clinical pharmacologists and microbiologists because antibiotic stewardship is teamwork, and cooperation between specialists is needed due to the high workload.

In Foolad et al.'s study, it was seen that the stewardship intervention increased antibiotic matching with guidelines (42% vs. 5.6%) and decreased the mean duration of antibiotic therapy[23]. prescribing the recommended antibiotic according to the protocol reduces the treatment period and increases the effectiveness of the treatment, and the correct prescription can reduce the length of hospitalization or mortality.

The current study showed that the hospitalization duration was the longest in patients with HAP and the lowest in patients with CAP. This discrepancy seems to be because most hospital-acquired infections causing HAP are resistant bacteria requiring longer treatment. It was also seen in the current study that patients with HAAP, CAAP, and VAP had a higher mortality rate than other patients, which needs to be investigated in future studies because it is possible that these patients died in the current study for other reasons than Infectious disease.

Iftikhar et al. found that in a hospital in Pakistan, a total of 40.8% of antibiotic prescription errors were related to wrong dose (19.9%), wrong frequency (18.9%), and repeated treatment (18.1%). Most of these errors were observed in the records of patients with long hospital stays (53.1%) [11]. This finding was in contrast with the findings of Hasler et al.'s study because Hasler et al. observed that prescription errors were corrected over time, although this difference between these two studies should be investigated in future studies [21]. The differences between the results of the Iftikhar et al. study and our study were that in our study, it was seen that the wrong dose and type of drugs were prescribed in 13.88% of cases, and in 31.94%, the wrong type of antibiotic was prescribed; but both studies showed that

mismatched prescription of antibiotic based on protocol had a high rate in hospitals.

In the study by Robert et al. in 2021, which evaluated the accuracy of prescribed antibiotics in CAP patients, it was seen that 80% of cases prescribed antibiotics were wrong (44). Wrong prescriptions did not affect mortality, but antibiotics were correct in only 20% of cases. This study highlights the need for a serious strategy to reduce prescription mismatch based on the ATS guideline. The result of this study is very different from the current study regarding the percentage of prescription errors (31.94% vs. 80%).

It is suggested that patients with pneumonia be evaluated regarding the correctness of the prescribed antibiotics, especially in all hospital wards except the infectious disease ward, where patients are only consulted by the infectious disease service. This assessment can be done daily by an infectious disease specialist or pharmacist. It is recommended that future studies with more statistical population be conducted on the causes of wrong prescription of antibiotics as well as the evaluation of the continuation of treatment, including the de-escalation of antibiotics according to the clinical status and fluid culture of the patient and the evaluation of the duration of hospitalization.

Conclusion

In this study, it was seen that 31.94% of patients with pneumonia who were admitted to Loghman Hakim Hospital in 2021 had wrong prescribed antibiotics. This wrong prescription was based on the wrong prescription of the type of antibiotic or its dose, and it was seen that among the patients who had a wrong prescription (31.94%), all of them had the wrong type of antibiotic prescription, and in 13.88%, the type and the dose of antibiotic at the same time was wrong. These numbers were lower compared to some studies in developed or developing countries, but they still remind us of the need for more attention to correct this process.

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None.

Conflict of interest

The authors further declare that they have no conflict of interest.

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