

# Economic Burden Of Inappropriate Empiric Antibiotic Therapy: A Report From Southern Iran

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**Introduction:** Widespread inappropriate antibiotic prescribing by healthcare professionals in the hospital setting is a great concern that may cause many undesirable consequences. Adherences to antibiotic guidelines have proven to be a simple and effective intervention to guide the choice of appropriate empiric antibiotic regimens and reduce the unnecessary variations in the practice among practitioners. The objective of this study was to evaluate the prescription patterns of empiric antibiotic therapy in relation to treatment guidelines and the economic burden of discordance with guidelines in a major referral Iranian university hospital.

**Method:** Hospital records of hospitalized patients with empiric antibiotic prescription, from September 2016 to February 2017 were reviewed. The process consisted of comparing empiric antimicrobial administration with institutional guidelines for each patient by a clinical pharmacist and an infectious disease specialist to evaluate the appropriate utilization of antibiotics. Adherence to guideline, the cost of antibiotics usage for each patient and the excess cost consequent from discordance with guideline was calculated.

**Results:** The most inappropriate prescribed antibiotics were carbapenems and aminoglycosides. Overall guideline adherence was 27.8%. Frequency of antibiotic usage incompatibility with the guidelines on the basis of dosing interval, duration of therapy and drug indication were 31.46%, 29.44% and 19.36%, respectively. General surgery and internal medicine wards had the least and the most inappropriate antibiotic administration, respectively. Totally antibiotic usage cost was 578,959.39 USD (24,316,294,800 Iranian Rials, IRR) for 6 months, which the excess costs of inappropriate antibiotic prescribing, was 471,319.69 USD (19,795,427,225 IRR). The estimated annual excess cost is 942,639.38 USD (39,590,854,450 IRR).

**Conclusion:** In this research, physicians' adherence with guidelines for empiric antibiotic therapy was low which was led to 471,319.69 USD excess costs. These results urge institution policy makers to develop guidelines to ensure active dissemination and implementation of them to decrease inappropriate antibiotic usage.

**Keywords:** inappropriate antibiotic usage, consumption, hospital, economic burden

## Introduction

Antibiotics are one of the most commonly prescribed drugs for the hospitalized patients. According to the previous studies, about one-third to one-half of all hospitalized patients receive antimicrobial therapy, which accounts for up to 30% of hospital drug budgets.<sup>1-3</sup> Hospitals all over the world are faced with the rapid emergence and spread of antibiotic-resistant bacteria. Increasing rates of antibiotic resistance have contributed to the greater recognition of inappropriate antimicrobial treatment for hospital-acquired infections.<sup>4</sup>

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To minimize inappropriate antimicrobial agent usage, clinicians must ensure that antibiotic administration follows certain minimal requirements, such as choosing an appropriate empiric therapy, considering accepted guidelines, proper dosing, optimal duration of treatment and changing treatment based on the subsequent culture results and antibacterial susceptibilities.<sup>5-8</sup>

Lack of adherence to these requirements based on antibiotic guidelines can lead to suboptimal or excessive antibiotic usage that increases the likelihood of antibiotic resistance, toxicity, and ineffective therapy.<sup>9,10</sup> Several strategies have been suggested for controlling antibiotic usage including formulary restriction, review and feedback strategies, educational programs, implementation of clinical guidelines, antibiotic cycling and antibiotic order forms.<sup>11-13</sup>

Application of the clinical guidelines can contribute to an appropriate selection of empiric antibiotic regimens and also reduce the unnecessary variations in the treatment of different infectious diseases.<sup>14,15</sup> According to the different patterns of antimicrobial sensitivity in hospitals, many hospitals have tried to develop their local guidelines based on the published international ones.<sup>16</sup>

Different studies have evaluated the overuse of antibiotics<sup>17-19</sup> and only limited ones have studied the economic burden of inappropriate prophylactic antibiotic usage in Iran.<sup>19</sup> As far as we know, there is no published research regarding the economic burden of inappropriate empiric antibiotic therapy from Iran. The objective of this study was to evaluate the prescription patterns of empiric antibiotic therapy in relation to treatment guidelines and the economic burden of discordance with guidelines in a major referral Iranian university hospital in southern Iran, Shiraz.

## Methods

### Study Population

We conducted a prospective observational study within 6 months from September 2016 to February 2017, in Shahid Faghihi hospital which is a tertiary referral teaching hospital affiliated to Shiraz University of Medical Sciences, Shiraz, Iran with about 42,000 admissions per year and 376 beds capacity. All patients who were hospitalized in the wards of internal medicine, general surgery, internal intensive care unit (ICU) and surgical ICU with antibiotic prescription were included in this study. Patients admitted to neurology and cardiology units were excluded because

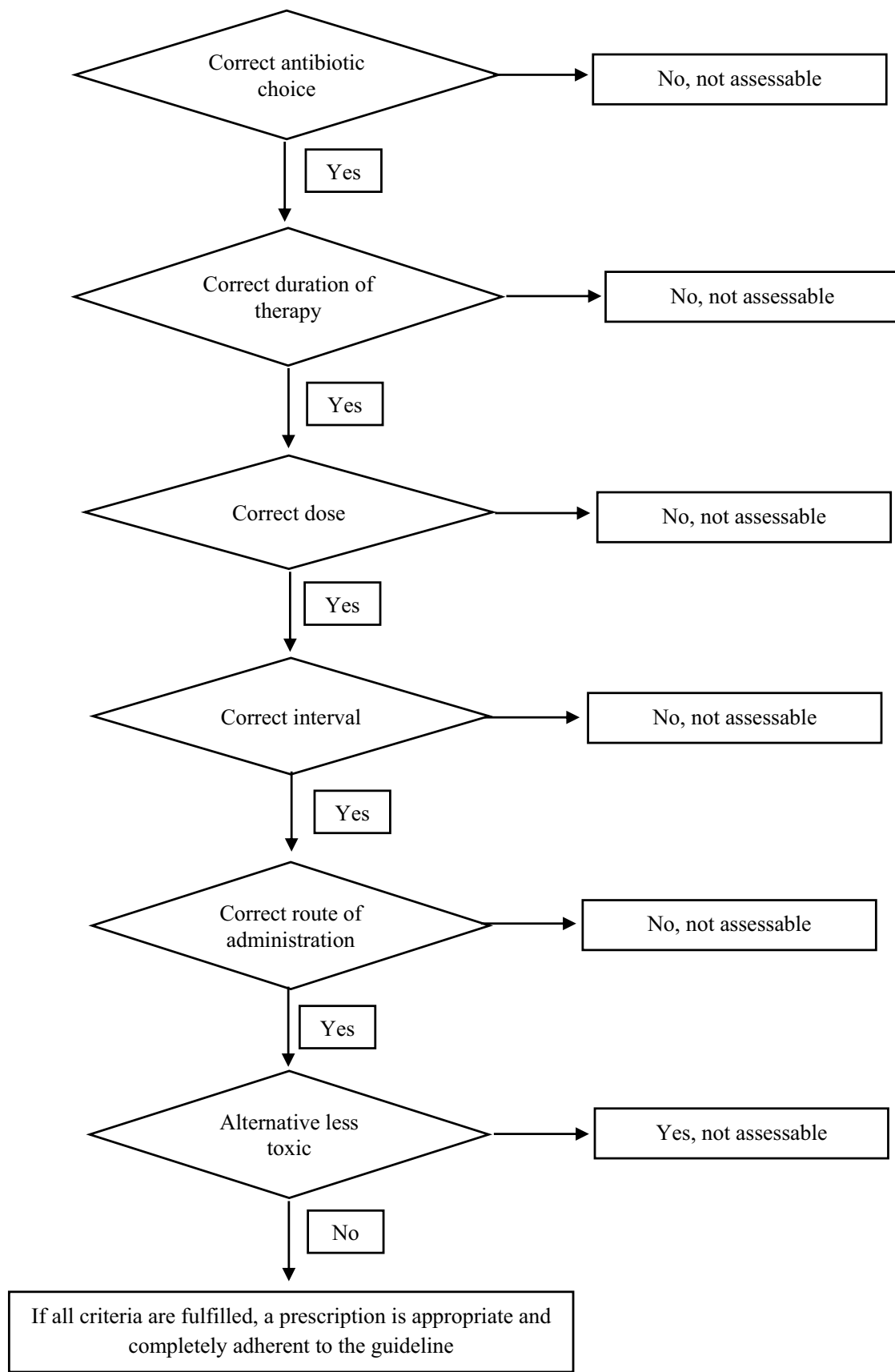
of their infrequent use of antibiotics. All studied patients were followed until the end of their antibiotic treatment. Being confirmed to have no infectious disease after 48 hours, having more than one infection, receiving prophylactic antibiotic regimens, expiring in the first day of admission and absence of enough information for a complete evaluation of patients' treatment course were exclusion criteria.<sup>20</sup> For each patient, demographic variables, laboratory and clinical data were recorded. The high accurate hospital records of each patient were evaluated because each drug requested for each patient had been recorded in the hospital information system (HIS). All medical and pharmacological records and all inpatient records related to antibiotic administration and starting or stopping dates of each drug were evaluated during the study period.

### Adhering Assessment

The primary outcome was the rate of inappropriate antibiotic prescribing. The process consisted of comparing empiric antimicrobial administration with institutional guidelines for each patient by a clinical pharmacist and an infectious disease specialist to evaluate the appropriate utilization of antibiotics. For this purpose, the quality of antibiotics prescription was assessed by using an algorithm (Figure 1) designed according to the method of van der Meer and Gyssens.<sup>21</sup> The appropriateness of the criteria mentioned in this algorithm was evaluated for each antibiotic according to institutional guidelines provided under the guidelines of the Infectious Diseases Society of America (IDSA)<sup>22</sup> and the US Centers for Disease Control and Prevention (CDC),<sup>23</sup> by the side of local microbial susceptibility patterns and hospital drug formulary.

### Cost Evaluation

The total cost of antibiotics was calculated using the hospital pharmacy computer system and data was collected from the HIS. The costs evaluated in this study were pharmaceutical costs that included both the cost of the health system and the cost of the patient. The excess cost was computed according to the percentage of any referent inappropriate antibiotic usages. Costs are reported in Iranian Rials (IRR) and US dollars (USD), by a conversion rate of 1 USD = 42,000 IRR. This conversion factor is based on the currency index allocated by the Central Bank of the Islamic Republic of Iran for the supply of medicine and medical equipment. The amounts of



**Figure 1** Assessment criteria for the evaluation of the quality of antibiotics prescription.

antibiotics administration are documented in total doses and DDD/100 patients/day for each antibiotic.

## Ethics Approval And Informed Consent

Institutional review board committee approval was obtained from the Shiraz University of Medical Sciences Ethics Committee (91-01-36-4872) and written informed consent was collected from patients. This study was conducted in accordance with the Declaration of Helsinki.

## Data Analysis

Data analysis was performed by SPSS version 17 software package (SPSS Inc., Chicago, IL, USA). The quantitative data were reported as mean  $\pm$  standard deviation (SD) and qualitative variables were presented by their frequencies and percentages. The odds ratios (ORs) and 95% confidence intervals (CIs) were used to evaluate the association between antibiotics and their appropriate use by employing a logistic regression model. Categorical variables were compared by using Chi-square test. Binary logistic regression was conducted separately for the infections and wards evaluated. The wards and infections were compared regarding inappropriate antibiotic administrations using crosstab test. A P-value  $<0.05$  was considered significant.

## Results

Among the evaluated patients, 229 patients met the inclusion criteria; 115 males (50.2%) and 114 females (49.8%). The average of the patients' age was  $56.42 \pm 19.54$ , ranging from 18 to 99 years. Demographic and clinical data of the patients are shown in Table 1. Cardiovascular diseases (81 patients, 35.3%) and diabetes mellitus (69 patients, 30.1%) were the most frequent pre-existing diseases.

A total of 493 antibiotics were prescribed for the evaluated patients during the study. The most frequently prescribed antibiotics were cephalosporins, carbapenems and glycopeptides which comprised 116 (23.5%), 78 (15.8%) and 66 (13.4%) of total prescriptions, respectively. Among these, aminoglycosides (100%) and carbapenems (97.43%), had the most and miscellaneous antibiotic group (42.10%) had the least proportions of inappropriate administrations (Figure 2, Table 2).

Among prescribed antibiotics, azithromycin (53.8%) and metronidazole (42.1%) were the most compatible antibiotics with the guidelines, whereas imipenem, amikacin and piperacillin-tazobactam were the most incompatible ones (all of them 100%). The best adherence to the guideline was in peritonitis and surgical site infections, while

**Table 1** Demographic And Clinical Data Of The Patients (n=229)

Variable	n(%) Or Mean $\pm$ SD
Sex	
Male	115(50.2)
Female	114(49.8)
Age (years)	56.42 $\pm$ 19.54
BMI (kg/m <sup>2</sup> )	23.69 $\pm$ 3.65
Duration of hospitalization (days)	12.28 $\pm$ 9.47
Duration of antibiotic treatment(days)	10.43 $\pm$ 7.28
Clearance of creatinine (mL/min)	
>90	54(23.6)
50–89	80(34.9)
10–49	75(32.8)
Hemodialysis	20(8.7)
Pre-existing medical diseases	
Cardiovascular diseases	81(35.3)
Diabetes mellitus	69(30.1)
Renal diseases	26(11.3)
Pulmonary diseases	18(7.8)
Cancers	12(5.2)
CNS diseases	5(2.1)
Gastrointestinal	5(2.1)
<sup>a</sup> Others	10(4.3)
Wards	
Internal medicine	115(50.2)
General surgery	61(26.7)
Internal ICU	34(14.8)
Surgical ICU	19(8.3)

**Notes:** <sup>a</sup>Others: psychiatric diseases, acquired immune deficiency syndrome (AIDS), hepatitis B, hepatitis C, rheumatoid arthritis and thyroid disorders.

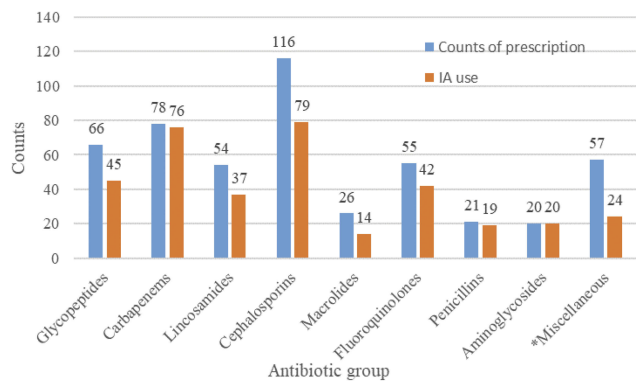
**Abbreviations:** SD, standard deviation; BMI, body mass index; CNS, central nervous system.

pyelonephritis and meningitis had the lowest compatibility with the guidelines (Both 0%) (Table 3).

Antibiotics were used least inappropriately in general surgery wards (52.8%), whereas the internal medicine wards had the most inappropriate usage of antibiotics (80.9%) (Table 4).

Comparison of antibiotics administrations appropriateness, regarding various aspects is shown in Table 5. Most of the prescription appropriate cases were related to route of administration, while the least appropriateness was due to dosing intervals.

In this study, the overall adherence of antibiotics regimen to the guidelines was 27.8%. The main aspects of inappropriate antibiotic usage were dosing interval, duration of therapy, and drug indication which were incorrect



**Figure 2** The appropriateness of antimicrobial therapy in different groups of antibiotics. **Note:** \*Miscellaneous included metronidazole. **Abbreviation:** IA, inappropriate administration.

in 156 (31.46%), 146 (29.44%) and 96 (19.36%) of prescribed ones, respectively.

Based on the patients’ renal function, dosing interval of 108 (21.9%) and dose of 38 (7.7%) antibiotics must be adjusted, but just 37 (34.2%) and 10 (26.3%) of these antibiotics met the correct adjustment for dosing interval and dose, respectively.

According to the culture results, the antibiotic regimen was de-escalated in 41 cases out of 85 positive cultures, whereas in 44 cases the modification was not suitable (Figure 3).

As it is shown in Table 6, total antibiotic use was 248.56 DDD/100 patients/day, while the most frequent-used antibiotic was ceftriaxone, 98.692 DDD/100 patients/day.

The total cost of antibiotics during our study was 578,959.39 USD (24,316,294,800 IRR) and the excess cost due to inappropriate antibiotic administration was 471,319.69 USD (19,795,427,225 IRR), equal to 81.41%

**Table 2** The Appropriateness Of Antimicrobial Therapy In Different Groups Of Antibiotics

Antibiotic Group	Frequency Of Prescription n (%)	AP Use n (%)	IA Use n (%)	P-Value	OR For IA Use (95% CI)
Glycopeptides	66 (13.4)	21 (31.9)	45 (68.1)	0.433	0.799 (0.456–1.399)
Carbapenems	78 (15.8)	2 (2.6)	76 (97.4)	<0.001	18.321 (4.433–75.719)
Lincosamides	54 (11)	17 (31.5)	37 (68.5)	0.521	0.819 (0.444–1.509)
Cephalosporins	116 (23.5)	37 (31.9)	79 (68.1)	0.259	0.771 (0.490–1.212)
Macrolides	26 (5.2)	12 (46.2)	14 (53.8)	0.036	0.426 (0.192–0.947)
Fluoroquinolones	55 (11.1)	13 (23.7)	42 (76.3)	0.467	1.276 (0.662–2.458)
Penicillins	21 (4.3)	2 (9.6)	19 (90.4)	0.075	3.806 (0.874–16.562)
Aminoglycosides	20 (4.1)	0 (0)	20 (100)	0.998	NC
<sup>a</sup> Miscellaneous	57 (11.6)	33 (57.9)	24 (42.1)	<0.001	0.228 (0.129–0.403)
Total	493 (100)	137 (27.8)	356 (72.2)		

**Note:** <sup>a</sup>Miscellaneous includes metronidazole.

**Abbreviations:** AP, appropriate; IA, inappropriate; OR, odds ratio; CI, confidence interval; NC, not calculable.

**Table 3** Adherence To The Guidelines For Antibiotic Therapy In Different Infections

Infection	Number Of Prescribed Antibiotics	AP Use n (%)	IA Use n (%)	P-value	OR For IA Use (95% CI)
CAP	96	16 (16.7)	80 (83.3)	0.008	2.192 (1.230–3.906)
Pyelonephritis	44	0 (0)	44 (100)	0.998	NC
Sepsis	73	13 (17.8)	60 (82.2)	0.042	1.933 (1.024–3.649)
Septic arthritis	16	7 (43.8)	9 (56.2)	0.156	0.482 (0.176–1.320)
HAP	25	4 (16.0)	21 (84.0)	0.186	2.084 (0.702–6.187)
Meningitis	4	0 (0)	4 (100)	0.998	NC
Cellulitis	16	2 (12.5)	14 (87.5)	0.183	2.763 (0.620–12.321)
Cholecystitis	40	11 (27.5)	29 (72.5)	0.966	1.016 (0.493–2.095)
Diabetic foot	38	16 (42.1)	22 (57.9)	0.044	0.498 (0.253–0.980)
SSI	24	12 (50)	12(50)	0.016	0.363 (0.159–0.830)
Abscess	18	7 (38.9)	11 (61.1)	0.289	0.592 (0.225–1.560)
Aspiration pneumonia	26	11 (42.3)	15 (57.7)	0.095	0.504 (0.225–1.126)
Peritonitis	73	38 (52.1)	35 (47.9)	<0.001	0.284 (0.170–0.474)
Total	493	137 (27.8)	356 (72.2)		

**Abbreviations:** AP, appropriate; IA, inappropriate; OR, odds ratio; CI, confidence interval; NC, not calculable; CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; SSI, surgical site infection.

**Table 4** The Appropriateness Of Antimicrobial Therapy In The Evaluated Wards

Ward	Number Of Prescribed Antibiotics	AP Use n (%)	IA Use n (%)	P-Value	OR For IA Use (95% CI)
Internal medicine	241	46 (19.1)	195 (80.9)	<0.001	2.396 (1.588–3.616)
General surgery	127	60 (47.2)	67 (52.8)	<0.001	0.298 (0.194–0.457)
Internal ICU	82	17 (20.7)	65 (79.3)	0.120	1.577 (0.887–2.801)
Surgical ICU	43	14 (32.6)	29 (67.4)	0.466	0.779 (0.389–1.524)
Total	493	137 (27.8)	356 (72.2)		

**Abbreviations:** AP, appropriate; IA, inappropriate; OR, odds ratio; CI, confidence interval; NC, not calculable; ICU, intensive care unit.

**Table 5** Comparison Of Antibiotics Administrations Appropriateness, Regarding Various Aspects

Antibiotics	Frequency Of Administration	Proper Safety n (%)	Appropriate Route Of Administration n (%)	Appropriate Interval n (%)	Appropriate Dose n (%)	Appropriate Duration n (%)	Appropriate Indication n (%)
Amikacin	20	4 (20%)	20 (100%)	12 (60%)	17 (85%)	11 (55%)	12 (60%)
Ampicillin-sulbactam	7	6 (85.7%)	7 (100%)	3 (42.9%)	7 (100%)	4 (57.1%)	3 (42.9%)
Azithromycin	26	26 (100%)	26 (100%)	25 (96.2%)	16 (61.5%)	22 (84.6%)	26 (100%)
Cefepime	7	6 (85.7%)	7 (100%)	2 (28.6%)	7 (100%)	6 (85.7%)	7 (100%)
Ceftazidim	6	5 (83.3%)	6 (100%)	3 (50%)	5 (83.3%)	6 (100%)	6 (100%)
Ceftriaxone	103	103 (100%)	103 (100%)	44 (42.7%)	97 (94.2%)	82 (79.6%)	98 (95.1%)
Ciprofloxacin	56	41 (73.2%)	45 (80.4%)	41 (73.2%)	47 (83.9%)	38 (67.9%)	44 (78.6%)
Clindamycin	55	55 (100%)	53 (96.4%)	52 (94.5%)	53 (96.4%)	35 (63.6%)	32 (58.2%)
Cloxacillin	8	8 (100%)	8 (100%)	4 (50%)	2 (25%)	7 (85.7%)	5 (62.5%)
Imipenem	62	0 (0%)	62 (100%)	40 (64.5%)	35 (56.5%)	34 (54.8%)	55 (88.7%)
Meropenem	16	11 (68.75%)	16 (100%)	7 (43.8%)	12 (75%)	12 (75%)	13 (81.3%)
Metronidazole	57	57 (100%)	56 (98.2%)	57 (100%)	57 (100%)	47 (82.5%)	39 (68.4%)
Piperacillin-tazobactam	6	6 (100%)	6 (100%)	5 (83.3%)	3 (50%)	4 (66.7%)	3 (50%)
Vancomycin	67	57 (85.07)	67 (100%)	45 (67.2%)	63 (94%)	42 (62.7%)	57 (85.1%)
Total	496	385 (77.62%)	482 (97.18%)	340 (68.54%)	421 (84.88%)	350 (70.56%)	400 (80.64%)

of the total cost. The estimated annual excess cost is 942,639.38 USD (39,590,854,450 IRR) (Table 7).

## Discussion

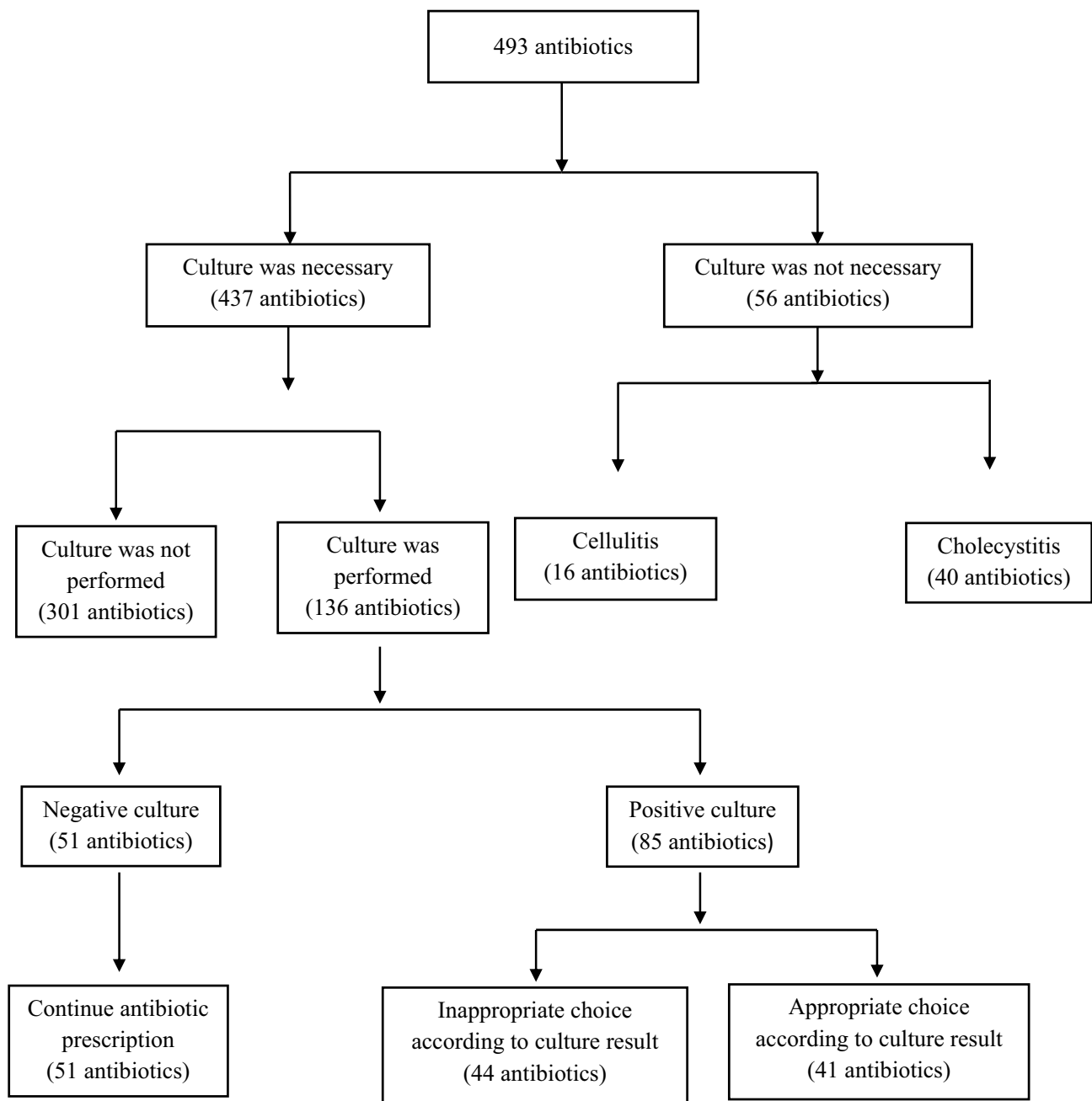
To the best of our knowledge, this is the first study from Iran to the economic consequence of inappropriate empiric antibiotic prescription at the hospital level as well as at the ward level. This hospital receives patients from a variety of healthcare settings and hospitals in south-west of Iran. Thus, we believe that our results are largely representative of tertiary care facilities of our country.

Despite guidelines which lead clinicians to prescribe appropriate empiric antimicrobial therapy to the hospitalized patients, growing literature show the inappropriate initial antimicrobial treatment.<sup>9,10</sup> A major concern is the increased use of broad-spectrum or new antibiotics and the prolonged use of antibiotics for empiric therapy. Physicians' adherence to local or hospital guideline is very important for the effective and

appropriate use of medications.<sup>5–8</sup> In our study, the total adherence (appropriateness of antimicrobial agent, de-escalation based on culture results, duration of treatment, route of antibiotic administration) with guidelines in empirical antibiotic treatment was found in 27.8% of patients.

As is shown in Table 6, antibiotic consumption in our report is relatively high, comparing to studies in developed countries. This may underscore the need of adherence to guidelines in developing countries. In addition, high use of some antibiotics may be due to differences in the epidemiological status of antimicrobial resistance. Carbapenems administration in Turkish hospitals with bed capacity < 500, was reported to be 32.8 DDD/1000 patient-days.<sup>24</sup> In another study in French hospitals, this rate of use was stated to be 3.7 DDD/1000 patient-days.<sup>25</sup> This rate was much higher in our study than reported in these studies (Table 6, 30.77 DDD/100 patient-day). Surprisingly, piperacillin-tazobactam consumption in Turkish report was 22.6





**Figure 3** Performing culture and modifying antibiotic regimens according to the culture results.

DDD/1000 patient-day,<sup>24</sup> while this rate was 1.373 DDD/100 patient-day in our research (Table 6).

Glycopeptides usages in 530 French hospitals were 6.7 DDD/1000 patient-day,<sup>25</sup> however vancomycin, as the only glycopeptide in Iran, was administered 34.22 DDD/100 patient-day in our research. The high proportion of vancomycin use in the present study may be explained by the epidemiological status of antimicrobial resistance. The high rate of resistance to methicillin in *Staphylococcus aureus* is reported in our country.<sup>26</sup>

As it is mentioned, some antibiotics have more frequent consumption comparing to developed countries, while some are administered less. World Health Organization (WHO) published a report, expressing antibiotic use in Iran as 38.78 DDD/1000 inhabitant day in 2015.<sup>27</sup> However, total antibiotic consumption in our study was 248.56 DDD/100 patient-day. Then, antibiotic use in our hospital did seem to be higher than some reports in other countries or also from the average of our own country.

**Table 6** Antibiotic administrations in DDD/100 patients/Day

Antibiotic	DDD/100 Patients/Day
Amikacin	1.958
Ampicillin-sulbactam	11.272
Azithromycin (oral)	8.945
Cefepime	1.286
Ceftazidime	0.613
Ceftriaxone	98.692
Ciprofloxacin (parenteral)	2.149
Clindamycin (parenteral)	19.375
Cloxacillin (PO)	6.653
Imipenem	15.77
Meropenem	14.999
Metronidazole	31.259
Piperacillin-tazobactam	1.373
Vancomycin	34.22
Total	248.56

Considering the pattern of use, the present study showed a high consumption of total antibiotics, which can be due to different reasons for this inappropriate use.

We found a significant overuse of antimicrobials that were clearly not indicated in more than 49% of cases. In the present study, 72.2% of total antibiotic prescriptions were incompatible with guidelines (Tables 2–4). As shown in some reports, the lack of indication is a popular reason for inappropriate use of antibiotics.<sup>20,28,29</sup>

Carbapenems and aminoglycosides were reported to be used the most inappropriately in the present study (Table 2). The most inappropriate prescribed antibiotic

groups reported in various studies are different based on the country and centers in which each study has been done.<sup>29–31</sup>

Use of broad-spectrum antimicrobials for empiric management of infections may be initially necessary. However, antimicrobial de-escalation is a key approach to balance the need of broad-spectrum initial treatment while limiting the emergence of antimicrobial resistance.<sup>32</sup> De-escalation requires that the initial regimen is subsequently narrowed after the pathogen and its antibiotic susceptibility are known. Besides, antimicrobial treatment is needed to be discontinued when the signs and symptoms of infection resolve. The present research showed that in 48.23% of cases the culture results were incorporated in antibiotic selection mostly in internal ICU and the least attention was paid in general surgery ward (Table 8). The notable point is that antibiotic choice according to culture results was inappropriate in 51.76% of positive cultures (Figure 3).

In a report from 323 hospitals of USA received in 2010, the common deviations from accepted protocols were missing of de-escalation, administering longer than needed, antibiotic prescription for nonbacterial infections and treating contaminations or colonizations.<sup>33</sup>

Medical records of patients with positive blood culture in a tertiary university hospital in Norway affirmed that 97% received empirical treatment at the time of culture report. Among these patients, 26% continued it, as being appropriate and 73% needed an adjustment, of which 12.05% did not meet this need.<sup>5</sup>

**Table 7** Total Costs And Waste Costs For Each Antibiotic

Antibiotic	DDD/100 Patients/Day	Total Cost (IRR)	Total Cost (\$)	IA (%)	Waste Cost (IRR)	Waste Cost (\$)
Amikacin	1.958	27,708,000	659.71	100	27,708,000	659.71
Ampicillin-sulbactam	11.272	624,368,000	14,865.90	85.7	535,083,376	12,740.08
Azithromycin	8.945	31,318,000	745.67	53.8	16,849,084	401.17
Cefepime	1.286	139,664,000	3,325.33	85.7	119,692,048	2,849.81
Ceftazidime	0.613	38,325,000	912.5	66.7	25,562,775	608.64
Ceftriaxone	98.692	2,056,650,000	48,967.86	67	1,377,955,500	32,808.46
Ciprofloxacin (Parenteral)	2.149	5,065,068,000	120,596.86	76.3	3,864,646,884	92,015.40
Clindamycin	19.375	1,266,680,800	30,159.07	68.5	867,676,348	20,658.96
Cloxacillin	6.653	210,748,000	5,017.81	87.5	184,404,500	4,390.58
Imipenem	15.77	5,785,120,000	137,740.95	100	5,785,120,000	137,740.95
Meropenem	14.999	5,063,850,000	120,567.86	87.5	4,430,868,750	105,496.87
Metronidazole	31.259	927,660,000	22,087.14	42.1	390,544,860	9,298.69
Piperacillin-tazobactam	1.373	227,035,000	5,405.59	100	227,035,000	5,405.59
Vancomycin	34.22	2,852,100,000	534,836.25	68.1	1,942,280,100	46,244.76
Total		24,316,294,800	578,959.39		19,795,427,225	471,319.69



**Table 8** Culture Practice Rates In Different Wards

Wards	Need The Culture To Be Performed	Culture Performed	Culture Was Not Performed	P-value
Internal ICU	81	63 (77.8%)	18 (22.2%)	<0.001
Internal medicine	223	44 (19.7%)	179 (80.3%)	
Surgical ICU	36	5 (13.9%)	31 (86.1%)	
Surgery	96	12 (12.5%)	84 (87.5%)	
<b>Total</b>	<b>436</b>	<b>124 (28.4%)</b>	<b>312 (71.6%)</b>	

Erbay et al stated that 45.3% of empiric regimens were inappropriate and generally, empirically antibiotic orders were less appropriate than those administered after culture tests.<sup>29</sup>

Antibiotics overuse, consequent from non-adherence to antibiotic guidelines, may cause an increase in direct cost of treatment. Furthermore, inappropriate use of antibiotics can lead to an increase in bacterial resistance and length of hospital stay. Our findings showed that the excess cost because of inappropriate antibiotic usage was 471,319.69 USD (19,795,427,225 IRR, Table 7) among 229 patients. In this study, 81.41% of total costs were due to the mis-prescription of antibiotics, which is a considerable rate. The increasing cost of antibiotics due to inappropriate usage has been addressed in number of studies.<sup>34-36</sup>

Such hospital-level analysis is useful for feedback to physicians in order to target key areas for improved performance. However, this research had some limitations, as there was not a feasible method to evaluate the clinical outcomes. Therefore, some conclusions about the inappropriateness of antibiotic therapy duration might not be drawn correctly. Also, there are different factors that affect an appropriate prescription, including the presence of clinical pharmacists, educational factors, and availability of antibiotics. The influence of these factors was not examined in our study, and prophylactic regimens were not evaluated.

## Conclusion

Antibiotic therapy inappropriateness is a widespread matter which is intended to be decreased by designing different guidelines. Though this ongoing issue is responsible for increasing antibiotic resistance all over the world yet. In this research, the high rate of incompatibility with the guidelines confirms the necessity of a closer monitoring of antibiotics administration, culture tests and appropriate sampling. The authors believe that there is a crucial need in incorporating evidence-based guidelines according to local conditions and cultural background in routine practice to improve patient safety and decrease direct costs in our hospital.

## Disclosure

The authors report no conflicts of interest in this work.

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