Costs of Appropriate and Inappropriate Use of Antibiotics in the Emergency Department

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ABSTRACT: **Background:** Appropriate antibiotic use is of both clinical and economic significance to any health system and should be given adequate attention. Prior to this study, no in-depth information was available on antibiotic use patterns in the emergency department of Hadassah Medical Center.

Objectives: To describe the use and misuse of antibiotics and their associated costs in the emergency department of Hadassah Medical Center.

Methods: We analyzed the charts of 657 discharged patients and 45 admitted patients who received antibiotics in Hadassah's emergency department during a 6 week period (29 April – 11 June 2007). A prescription was considered appropriate or inappropriate if the choice of antibiotic, dose and duration by the prescribing physician after diagnosis was considered suitable or wrong by the infectious diseases consultant evaluating the prescriptions according to Kunin's criteria.

Results: The overall prescribing rate of antibiotics was 14.5% (702/4830) of which 42% were broad-spectrum antibiotics. The evaluated antibiotic prescriptions numbered 1105 (96 prescriptions containing 2 antibiotics, 2 prescriptions containing 3 antibiotics), and 54% of them were considered appropriate. The total inappropriate cost was 3583 NIS (1109 USD PPP) out of the total antibiotic costs of 27,300 NIS (8452 USD PPP). The annual total antibiotic cost was 237,510 NIS (73,532 USD PPP) and the annual total inappropriate cost was 31,172 NIS (9648 USD PPP). The mean costs of inappropriate prescriptions were highest for respiratory (112 NIS, 35 USD PPP) and urinary tract infection (93 NIS, 29 USD PPP). There were more cases when the optimal cost was lower than the actual cost (N=171) than when optimal cost was higher than the actual cost (N=9). In the first case, the total inappropriate costs were 3805 NIS (1178 USD PPP), and in the second case, -222 NIS (68.7 USD PPP).

Conclusions: The use of antibiotics in emergency departments should be monitored, especially in severely ill patients who require broad-spectrum antibiotics and for antibiotics otherwise restricted in the hospital wards. Our findings indicate that 12% of the total antibiotic costs could have been avoided if all prescriptions were optimal.

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KEY WORDS: inappropriate cost, antibiotic prescribing, emergency department

As Sir Alexander Fleming predicted in his Nobel Lecture, antimicrobials – since their introduction – have been pivotal in the prevention and treatment of infections [1]. However, the increasing use of antimicrobials has led to a situation of appropriate and inappropriate use. Although there is no consensus on the definition of 'appropriate' therapy, "…Appropriate antimicrobial therapy implies that the indication, choice of drug, timing of administration, route, dosage, frequency and duration of administration have been rigorously determined" [2]. Allowance should also be made for switching broad empiric therapy to a narrower definitive treatment and from intravenous to oral drugs.

Appropriate antibiotic use is of both clinical and economic significance to any health system and should be given adequate attention. A previous study in northern Israel estimated that antibiotics prescribed for predominantly viral illnesses accounted for about a fifth of all emergency room antibiotic prescriptions [3].

In the emergency department, the meeting between patient and physician is often sporadic. In such cases, the patient's history may be lacking and antibiotic prescribing for infectious diseases is empiric. This can result in the use of broad-spectrum agents in order to cover all likely causative organisms and, subsequently, increased health care costs. Two Cochrane reviews were conducted on interventions to improve appropriate antibiotic use in ambulatory care and in the hospital, but neither addressed the unique setting of emergency medicine, most probably due to the scarcity of ED studies on prescribing practices, factors predicting antibiotic use/misuse, and interventions to improve judicious use of antibiotics [4,5].

NIS = New Israeli Shekel
USD PPP = US dollar purchasing power parity
ED = emergency department

A recent study by Shorr and colleagues [6] demonstrated that implementation of a protocol guiding the management of sepsis in the emergency department resulted in subsequent substantial cost savings and improved patient outcomes in the intensive care unit and other sections of the hospital. However, costs in the ED were not altered at all by the protocol. The protocol had appropriate antibiotic use at its core, and this demonstrates that even though antibiotic costs in the ED may seem minimal compared to overall antibiotic costs in the hospital, its effects can be far reaching.

Thus, the costs of antibiotic prescribing in the ED and the costs of inappropriate prescribing have ripple effects on both hospital and community health care costs. The aim of this study is to advance knowledge and provide information about ED antibiotic use and its costs, specifically:

- to compute and describe the distribution of costs of ED antibiotic prescriptions during the study period
- to compute and describe the distribution of costs of inappropriate prescriptions (inappropriate costs)
- to determine the association between the cost of inappropriate prescriptions and the antibiotics prescribed, the time of day, the day of the week, and the patient's age, gender and diagnosis.

METHODOLOGY

Hadassah Medical Center (Ein Kerem campus) is a university hospital with 700-bed tertiary care that serves as a national referral center for many complex and challenging medical cases. The ED has 30 adult beds and 8 pediatric beds and receives about 200 patients daily during the week and somewhat less at weekends.

In this descriptive cross-sectional study we conducted a retrospective analysis of antibiotic prescription appropriateness and an economic analysis of the antibiotic prescriptions in Hadassah's ED. The data collection period was from 29 April to 11 June 2006 (6 weeks) with an initial pilot data collection in early April 2006.

Antibiotics with activity against a wide range of microorganisms like Gram-negative bacteria, Gram-positive bacteria and atypical microorganisms were considered broad spectrum. The antibiotics evaluated as broad spectrum in this study included amoxicillin/clavulanic acid, ciprofloxacin, cefotaxime, ceftazidime, ceftriaxone, imipenem, meropenem and piperacillin/tazobactam.

Evaluation of appropriateness was carried out using a modification of Kunin's criteria. Named for its first use by Calvin Kunin, this methodology is based on local prescribing patterns and allows for individual evaluation of each prescription as opposed to developing general criteria/categories of infections and appropriate antibiotic use [7].

The categories of antibiotic use were developed by consensus among infectious disease consultants in the infectious disease department based on local patterns of antibiotic prescribing in Hadassah and also using a modification of Kunin's criteria. The categories of antibiotic use developed are as follows:

Category	Description
1	Correct choice of antibiotic, dosage, duration and route
2	Correct choice of antibiotic, disagree with dosage
3	Correct choice of antibiotic, disagree with duration
4	Correct choice of antibiotic, disagree with route
5	Disagree with chosen antibiotic because its spectrum is too broad
6	Disagree with chosen antibiotic because the spectrum it covers is too narrow or entirely wrong
7	No antibiotic treatment indicated
8	No conclusion possible with present data
9	Disagree with protocol

There was no evaluation when no antibiotic was given. A wrong spectrum implies that the antibiotic given does not correspond to the causative spectrum indicated by the diagnosis. "Protocol" is used when the antibiotic prescription is considered inappropriate but follows an emergency room protocol and cannot be attributed to an individual physician's judgment alone; for example, giving prophylactic antibiotics for lacerations. A prescription that falls into more than one category is classified into the category that best describes the antibiotic prescription

The study population comprised 702 patients to enable ample sample size for appropriateness analysis. A total of 490 patients were prescribed antibiotics in the emergency room, the others being prescribed antibiotics only on discharge. The cost analysis reflects the costs to Hadassah and thus refers to these 490 patients who received antibiotics in the ED (one patient with an outlier cost was excluded). The total number and costs of all drugs dispensed in the ED during the study period was obtained from Hadassah's pharmacy department.

Inappropriate costs were calculated as the difference between the costs of the actual antibiotic received and the costs of optimal antibiotic recommended during evaluation of the antibiotic prescriptions by the infectious disease consultant. Notice that the inappropriate cost could be either positive or negative. Those not included in the economic analysis included patients who did not receive antibiotics in the ED and those for whom antibiotics were only prescribed on discharge. Subsequent univariate analysis was carried out with independent variables using the ANOVA *F*-test. Details of the distribution of inappropriate costs was obtained and univariate analysis was conducted with independent variables using the non-parametric Kruskall-Wallis test .

RESULTS

During the study period 702 patients from a total of 4830 seen in the emergency room of Hadassah Medical Center were prescribed antibiotics. Antibiotics accounted for 18% of the total drug costs in the ED during the study period. Of the 24 antibiotics prescribed, 3 (cefuroxime, azithromycin and ciprofloxacin) accounted for 53% of the total antibiotic costs. The proportion of antibiotic costs from among all the drug costs was highest for the short admission/observation section of the emergency room. This section accounted for over a third of the total drug cost (36%) in the ED. Of the 702 patients included in the study, 490 were prescribed antibiotics in the emergency room. The total cost of antibiotics prescribed for these patients was 27,300 NIS (8452 USD PPP) [8]. The mean cost of treating a patient with antibiotics (excluding outliers) in the ED was 56 NIS (17 USD PPP).

In 36% of the patients seen in the emergency room (180/491), the antibiotics received were considered inappropriate and an optimal antibiotic was suggested. Altogether, 54% of patients received antibiotic therapies considered appropriate, while in other patients there were insufficient data for evaluating the given therapy (5%) or recommending an optimal antibiotic (5%).

For patients with inappropriate therapies, inappropriate costs were either negative or positive, ranging from -70 NIS (-22 USD PPP) to 211 NIS (65 USD PPP). The total inappropriate costs were 3583 NIS (1109 USD PPP) and the average cost of inappropriate antibiotic therapy during the study period was 20 NIS (6 USD PPP). Optimal costs were higher than the actual cost for 9 patients (5% of total inappropriate cases) and totalled -222 NIS (68.7 USD PPP) with a mean of 25 NIS (8 USD PPP), while the optimal cost was lower than the actual cost for 171 patients (95% of total inappropriate cases and totaling 3805 NIS (1178 USD PPP) with a mean of 22 NIS (7 USD PPP),

Antibiotic costs were distributed differently across categories of patients' age and gender, specialty of the prescribing physician, diagnostic tests ordered before the prescription was issued, the physician's final diagnosis of infection, and the class of antibiotic prescribed. These differences were statistically significant [Table 1]. The inappropriate costs – in the two cases – are presented in Table 2.

Since the number of cases whose optimal cost was higher than the actual cost may have been too few to deduce statistically significant differences, the discussion will focus on cases where optimal cost was lower than actual cost.

On analysis of inappropriate costs, differences in inappropriate costs remained statistically significant across categories of patients' age, specialty of the prescribing physician, diagnostic tests ordered before the prescription was made, physician's final diagnosis of infection, and class of antibiotic prescribed [Table 1].

It is noteworthy that internists had the highest mean antibiotic costs (129 NIS, 40 USD PPP) and inappropriate costs (84 NIS, 26 USD PPP) compared to other specialties. There was a monotonic increase in mean antibiotic costs across the age groups, with a fivefold difference (126:25) in mean antibiotic cost between youngest and oldest age groups. Inappropriate costs were also significantly different across age categories.

Prophylaxis and respiratory infections were the most frequent diagnoses leading to antibiotic prescriptions. Respiratory (141 NIS, 44 USD PPP) and urinary tract infections (109 NIS, 34 USD PPP) had the highest mean antibiotic costs compared to other diagnoses (11–87 NIS, 3–27 USD PPP). The same pattern was found for inappropriate costs. Antibiotic costs and inappropriate costs were not significantly different on the days of the week and times of day that the patients arrived at the ED.

DISCUSSION

The annual costs derived from the study results by multiplying the 6 week values by 8.7 (52/6) revealed that the annual total antibiotic cost was 237,510 NIS (73,532 USD PPP) and the annual total inappropriate cost was 31,172 NIS (9648 USD PPP). Patients who received antibiotics and for whom diagnostic tests were performed had significantly higher antibiotic costs when compared to those who had no diagnostic tests. This shows that some measure of caution is in place regarding the use of more expensive antibiotics compared to cheaper antibiotics. There was a statistically significant difference in distribution of inappropriate costs between categories of diagnostic tests. However, patients who had undergone diagnostic tests were more likely to be wrongly prescribed an expensive antibiotic, while patients who had not undergone diagnostic tests were wrongly prescribed cheaper antibiotics. In all identified cases where the optimal cost of an antibiotic was higher than the actual cost, diagnostic tests were not ordered. The use of diagnostic test results to aid in choosing an antibiotic in the ED should therefore be investigated in a more detailed study.

As stated earlier in the Results, prophylaxis was among the most frequent for an antibiotic order. As also observed in other studies in Israel [9,10], this has an implication for antibiotic resistance trends in the study population, considering the high use of prophylactic antibiotics in the emergency room.

Although the total antibiotic costs were moderate for patients diagnosed with ear, nose and throat infections as compared to other groups, the mean inappropriate cost was very high, probably because most upper respiratory infections are viral in origin and do not require antibiotics. One of the reasons is suboptimal diagnosis. Another is that patients put pressure on physicians to give them 'something' to relieve the discomfort from colds and other upper respiratory infections [4,5].

Physician specialty has been found to be predictive of antibiotic choice [6], and although the patients seen by different

Table 1. Description and distribution of antibiotic costs and inappropriate costs

			Innapropriate cost cases			
	Cost		Optimal cost lower than actual cost		Optimal cost higher than actual cost	
Total	**27,300 NIS**		**380 NIS**		**-222 NIS**	
	N	**Mean (NIS)**	**N**	**Mean (NIS)**	**N**	**Mean (NIS)**
Age (yrs)	‹ 0.0001*		‹ 0.0001		0.43	
0–9	133	25	51	13	3	-18
10–19	55	24	35	12	1	-1
20–29	76	47	26	19	1	-34
30–49	91	58	31	18	0	
50–69	66	75	16	58	0	
70+	68	126	12	63	4	-34
Gender	0.012		0.36		0.455	
Male	203	61	53	26	4	-17
Female	283	52	117	21	5	-31
Specialty	‹ 0.0001		‹ 0.0001		0.491	
Pediatric	66	41	8	45	0	
Surgery	171	19	109	10	2	-15
Internal	103	129	16	99	2	-43
Maxillofacial	61	20	27	7	2	-16
ENT	21	39	3	21	1	-1
Others	53	75	6	65	1	-50
Diagnostic test	‹ 0.0001		0.001			
No	211	24	106	12	5	-25
Yes	235	64	60	33	0	
Physicians' diagnosis	‹ 0.0001		‹ 0.0001		0.234	
Prophylaxis	172	11	136	7	2	-1
Skin, soft tissue and bone	78	41	10	37	2	-33
Ear, nose and throat	59	53	9	87	1	-1
Respiratory	667	141	7	138	1	-70
Urinary tract	42	109	4	93	0	
Maxillofacial	23	35	0		1	-30
Systemic & endovascular	30	85	2	119	2	-25
Gastrointestinal & others	15	87	2	47	0	
Antibiotic prescribed	‹ 0.0001		‹ 0.0001		0.189	
Narrow spectrum	304	22	141	12	6	-17
Broad spectrum	186	111	30	68	3	-40
Day patient arrived	0.413		0.746		0.81	
Sunday	86	44	30	28	1	-16
Monday	84	57	29	27	1	-51
Tuesday	64	47	19	24	2	-36
Wednesday	49	72	20	9	2	-11
Thursday	80	63	25	28	2	-16
Friday	56	48	26	13	0	
Saturday	71	63	22	24	1	-30
Time patient arrived	0.19		0.103		0.324	
Day (7:00-14:59)	172	61	58	26	3	-13
Evening (15:00-22:59)	224	49	82	17	4	-38
Night (23:00-6:59)	89	60	30	22	2	-15

**P* values obtained from Kruskall-Wallis non-parametric test. Since the distribution of inappropriate costs did not follow a normal distribution, analysis to determine statistically significant differences between categories of independent variables was carried out using a non-parametric test (Kruskall-Wallis for k-independent samples) and the *P* values obtained are reported

1 USD PPP = 3.23 NIS

Table 2. Lower optimal and higher optimal cost cases

Higher optimal cost cases	**N**	**9**
	Mean*	-24.7
	Mode	-1.3
	Minimum	-70.3
	Maximum	-1.3
	Sum	-222.1

Lower optimal cost cases	**N**	**171**
	Mean	22.3
	Mode	6.8
	Minimum	5.5
	Maximum	211.4
	Sum	3805.1

* All values are in NIS except for N, which denotes the number of patients

specialties have differing needs for antibiotics, this shows possible areas of intervention to promote appropriate and cost-effective antibiotic use. Consistent with this, Steinman and co-authors [11] found that internists were likely to choose broad-spectrum agents more often than general practice physicians and this could lead to higher antibiotic costs.

Davey and team [4] reviewed 66 studies to determine what intervention methods are effective, and they found that both persuasive methods (e.g., education) and restrictive methods (e.g., requirements for prior approval before prescribing certain antibiotics) had positive impacts on improving antibiotic-prescribing practices in hospitals. A recent study by Greene et al. [12] found that a multifaceted intervention – consisting of financial incentives, physician profiling and education – was effective in promoting appropriate prescribing through increasing adherence to recommended guidelines.

Physicians' diagnosis is obviously a factor that affects which antibiotic is prescribed, as also demonstrated in this study, and this underlines the importance of ruling out as much diagnostic uncertainty as possible to avoid overuse of antibiotics. The U.S. Food and Drug Administration suggests that local epidemiology and susceptibility patterns be made

available and updated regularly to aid in the empiric selection of antibiotic therapy [13].

The generalizability of these conclusions is uncertain, as the study reflects antibiotic prescribing practices in only one ED in Israel. Regional variations as well as other differences such as academic status and size of hospital may affect prescribing patterns. A nationally representative study may be necessary before policy decisions are made. In addition, generalization of the study results to annual prescribing practices at the Hadassah Medical Center should be done with caution due to the seasonal nature of some infectious diseases (especially respiratory tract infections). The study results are most probably an underestimation of overall (e.g., yearly) patterns of antibiotic use in Hadassah's ED as it was carried out in the summer months when colds and other viral respiratory tract infections leading to inappropriate antibiotic use are not as common. The results, however, indicate the need for educative and restrictive intervention in Hadassah's ED. In addition, in-depth studies on antibiotic prescribing in Hadassah's ED as well as in other wards in Israeli medical centers are recommended. In conclusion, high antibiotic costs follow high inappropriate costs, since the use of expensive antibiotics was unjustified more often than not.

Inappropriate use of antibiotics creates costs not only to the medical center where it occurs but also to society at large. Accumulated antibiotic resistance is one of the main factors for increased morbidity and health care costs.

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