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## Original Research

# Antibiotic Stewardship Program Experience in a Training and Research Hospital

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### Abstract

**Objectives:** Antibiotic Stewardship Programs (ASP) have been developed for the spread of rational antibiotic use. Our hospital is one of the first centers where ASP applications were launched in Turkey. In this study, we aimed to share our experience with ASP which has been applied in our hospital since 2013.

**Methods:** We adapted ASP to our hospital program from Centers for Disease Control and Prevention's ASP checklist. Revisions on surgical prophylaxis guidelines and practices were performed. Surgical prophylaxis was evaluated from hospital infection surveillance and antibiotic usage by point prevalence surveys. Antibiotic consumption indexes (ACI) were calculated from hospital pharmacy records. Rapid antigen detection test (RADT) for Group A beta-hemolytic streptococcus and influenza rapid antigen test were started to be used. Cumulative antibiotic susceptibility results were prepared annually.

**Results:** Surgical prophylaxis was started to be administered in the operating room within 60 min of incision. Third-generation cephalosporin usage for surgical prophylaxis could be restricted in all clinics but the duration could only be shortened in neurosurgery and general surgery. There was no statistically significant change in antibiotic usage rates and appropriateness between 2014 and 2018. ACI for the class J01 in adult wards was 80.5 daily defined doses (DDD) per 100 patient days in 2014 and reduced to 64.8 DDD per 100 patient days in 2018. 22.445 pediatric patients presenting with complaints of the upper respiratory tract were evaluated with RADT and 75.1% were treated without antibiotics.

**Conclusion:** In this global antimicrobial resistance era, all hospitals should have motivated antimicrobial stewardship teams. Each hospital should establish its own stewardship program and often revise it. Improvement in rational antibiotic use is hard to achieve without multidisciplinary involvement.

**Keywords:** Antibiotic stewardship program; antimicrobial resistance; rational antibiotic use.

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Microorganisms with multiple antibiotic resistances are an important public health problem, which has led to an increase in morbidity, mortality, and health

expenditures. The Infectious Diseases Society of America (IDSA) has been the first to introduce the appropriate antibiotic usage guideline in 1988 against antibiotic re-

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sistance. In addition to guidelines, national and international Antibiotic Stewardship Programs (ASP) have been developed.<sup>[1,2]</sup> The term “antimicrobial stewardship” was first used in 1996 in United States by McGowan Jr. and Gerding.<sup>[3]</sup> ASP is defined as the action plan which provides the appropriate use of antibiotics when necessary.<sup>[4,5]</sup> The main objectives of ASP are to determine the appropriate dosage, route, and duration of treatment, to prevent the spread of microorganisms with multiple drug resistance, to reduce the undesirable effects caused by irrational antibiotic use, and to reduce the high cost rates due to unnecessary antibiotic use.<sup>[1,6,7]</sup>

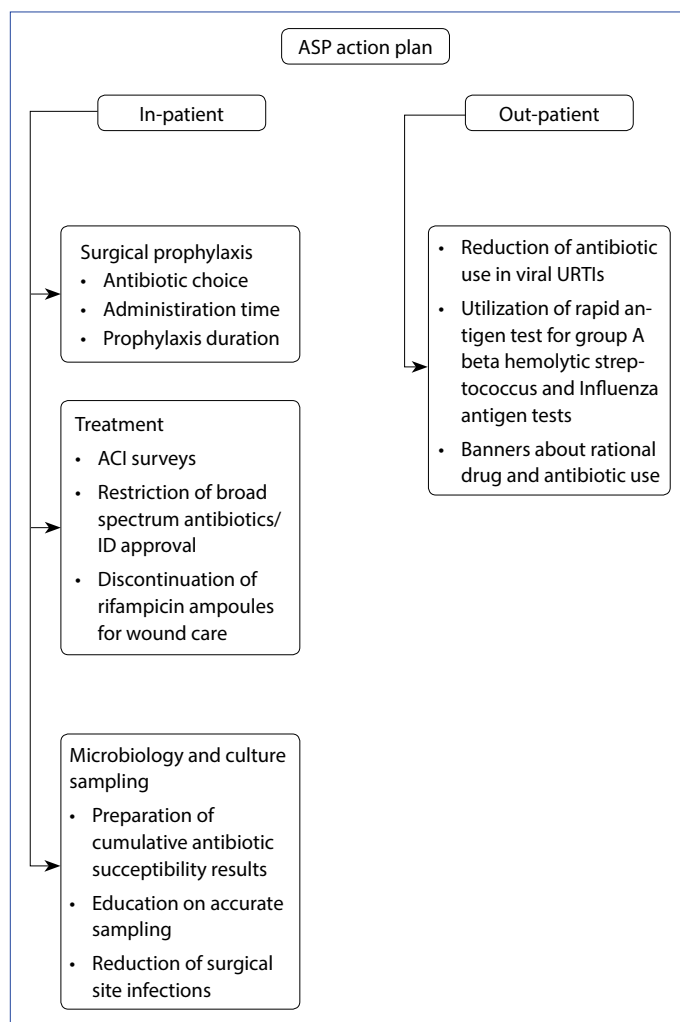
ASPs have been developed and implemented in many countries during the 1990s and 2000s. Our hospital is one of the first centers where ASP applications were launched in Turkey. In this study, we aimed to share and evaluate our experience with ASP which has been applied in our hospital since 2013.

## Methods

Our hospital is a tertiary teaching hospital with 798 beds (672 beds for adults and 126 beds for pediatric cases). In this study, we shared our 6 years of experience with the ASP, which was adapted to our hospital from Centers for Disease Control and Prevention (CDC)'s ASP checklist, applied by our Antibiotic Control Team (ACT).<sup>[8]</sup> Infection diseases specialist (IDS), clinical microbiologist, vice chancellor, chief pharmacist, clinical pharmacist, general surgeon, internal medicine specialist, anesthesiologist and reanimation specialist, infection control nurse, and Information Technologies expert took part in the team. The ACT made its first meeting in October 8, 2013, and continued to convene once a month or earlier. Figure 1 shows the low-hanging fruits and plan of our ASP. Physicians from certain clinics were invited to ACT meetings when a problem was detected about the antibiotic usage.

### Surgical Prophylaxis

First, studies on surgical prophylaxis and treatment protocols were performed by ACT. Surgical prophylaxis guideline of our hospital was renewed in collaboration with surgeons and was made easily visible through our hospital website institutional portal. Two different options such as “prophylactic” and “treatment” were submitted for electronic antibiotic orders to check up on the concept of prophylaxis and to question the purpose of giving antibiotics on a daily basis. To restrict ceftriaxone consumption, hospital information system was rearranged for the approval on the 1<sup>st</sup> day instead of the 3<sup>rd</sup> day by IDS. The major changes in prophylaxis guidelines were offering cefuroxime instead of cefazolin in urologic surgeries and



**Figure 1.** Our ASP action plan.

ACI: Antibiotic consumption index; URTI: Upper respiratory tract infection.

ampicillin sulbactam in biliary surgeries, if needed. Cefazolin was the choice for most clean and clean-contaminated surgeries.

It was observed that patients were brought to the operating room after surgical prophylaxis was performed in the wards. Urology Clinic was selected to examine the period between prophylactic antibiotic administration and incision, and it was found to be longer than 2 h in some cases. To achieve standardization, all surgical prophylaxis were started to be administered by the anesthesia team in the operating room within 60 min before surgical incision.

Global guidelines for the prevention of surgical site infection point out prolonged antibiotic prophylaxis exceeded 24 h after surgery has no advantage in surgical site infections.<sup>[9]</sup> We examined appropriate surgical antibiotic prophylaxis duration times and prophylactic antibiotic choices by previously determined surgical wards in 2014 and 2018 from surgical site infection surveillance data.

The clinics were chosen in terms of surgical site infection risk and the surgeries that we could exclude contaminated or dirty operations. Comparative surgical prophylaxis data with the previous months were given to the clinical chiefs, quarterly.

### **Antibiotic Usage**

Principles have been developed by the World Health Organization (WHO) for the prevention of inappropriate prescription of antibiotics.<sup>[10]</sup> Irrational antibiotic use is also serious public health problem which affects our country, too. The Ministry of Health in Turkey launched a nationwide antibiotic restriction program in February 2003. According to this program; anti-pseudomonal beta-lactamase inhibitors, intravenous third- and fourth-generation cephalosporins, carbapenems, parenteral quinolones, parenteral antifungals, anti-Methicillin-resistant *Staphylococcus aureus* (MRSA) agents (vancomycin, linezolid, and daptomycin), and polymyxins (colistin), new generation antibiotics such as tigecycline can only be used with IDS approval through a computerized pre-authorization system.

The current antibiotic usage and antibiotic applications in our hospital were discussed in the context of the guidelines.<sup>[11,12]</sup> Rearrangements have been made in the hospital information system related to antibiotic practices. A "Controlled Antibiotic Request Form" was created for antibiotic requests which need IDS approval. The differences between antibiotic usage rates and appropriateness among surgical and medical adult wards were evaluated by point prevalence surveys (PPS) in February 26, 2014 and January 23, 2018. Antibiotic consumption indexes (ACIs) were retrieved from hospital pharmacy records. ACIs of adult clinics were started to be analyzed to follow the results of rearrangements in treatment protocols and to compare our data with other hospitals. For this purpose, Anatomical Therapeutic Chemical (ATC) Classification/Daily Defined Doses (DDD) system, which is recommended by the WHO, was used.<sup>[13]</sup> ABC Calc version 3.1 was used for ACI calculation on a Microsoft Excel® application. This application converted the number of dispensed units (vials, pills, capsules, or bottles) into the number of DDD and then to the number of DDD/100 PD, as recommended by the WHO, following the 2006 version of ATC/DDD classification. The old DDD were used for 2018 calculation to compare the data with 2014.

Studies suggest that antibiotic use in viral upper respiratory tract infections is the most common cause of antibiotic misuse in out-patient clinics.<sup>[14-16]</sup> We aimed to reduce antibiotic prescribing rates in viral upper respiratory tract infections, mainly in emergency clinics. Thus, rapid antigen

detection test (RADT) for Group A beta-hemolytic streptococcus (GABHS) and influenza rapid antigen test (IRAT) were started to be used. Intramuscular benzathine penicillin was supplied from the hospital pharmacy to ensure the application of antibiotherapy for patients infected with GABHS. Antibiotic prescribing rates in acute tonsillopharyngitis were evaluated after RADT use.

### **Rifampicin**

Rifampicin is a valuable drug for the treatment of tuberculosis.<sup>[17]</sup> Rifampicin ampoules were frequently used in wound care in Physical Therapy and Rehabilitation, Neurosurgery, Orthopedics, and Plastic Surgery Clinics in our hospital. Interviews were conducted with these clinics to prevent local use of rifampicin ampoules for wound care. A local wound care guide prepared by ACT with the contribution of these departments.

### **Microbiology and Culture Sampling**

Cumulative local antibiotic susceptibility results were prepared annually according to guidelines.<sup>[18]</sup> These reports, which are guiding in empirical treatment, were shared on the hospital institutional portal and were announced to all doctors by e-mail.

Education on accurate sampling for cultures was given by Microbiology and Infectious Diseases Clinics to the related clinics. To reduce blood culture contamination rates, chlorhexidine and alcohol-containing wipes were put into the blood culture kits and given to the clinics (except for babies under 2 months).

In case of positive blood culture results, information was given to physicians by Microbiology Clinic.

### **Surgical Site Infections**

In line with the recommendations renewed in November 2016 by the WHO,<sup>[9]</sup> posters were created and hung in visible places in operating rooms. Guidelines for the treatment of complicated intra-abdominal infections have been prepared and shared with Adult and Pediatric Gastroenterology Clinics.

### **Data Analysis and Ethics Approval**

All statistical analyses were done using IBM SPSS Statistics, version 21.0. According to distribution of data, Student t or Mann-Whitney U-test were used. Chi-square and Fisher's exact tests were used for categorical variables as appropriate. All analyses were considered significant at  $p < 0.05$ . The study was assessed by the Regional Ethical Review Board in Sisli, Turkey on 16, April 2019, registration number 2347.

## Results

### Surgical Prophylaxis

Significant differences were observed in surgical prophylaxis applications through our ASP. When the clinics were evaluated separately, prophylactic ceftriaxone usage decreased from 49.3% in 2014 to 11.4% in 2018 in General Surgery Clinic; 7.8% to zero in Neurosurgery; and 30% to zero in Urology Clinic ( $p < 0.01$ ). In general surgery, this may be due to the change in surveyed operations, but Urology and Neurosurgery Clinics fully accepted the advised prophylactic agents. In Urology Clinic, as second-generation cephalosporins do not need IDS approval in our country, we could not achieve the appropriate duration and nearly all patients received

prolonged antimicrobial prophylaxis. Furthermore, the Gynecology Clinic started to use more prolonged prophylaxis; but we could not be successful in reducing unrestricted first-generation cephalosporin use although we gave multiple education and feedbacks. The Orthopedics and Traumatology Clinic changed their protocol and started to give ampicillin sulbactam following cefazolin. We could be able to restrict WHO watch group antibiotics for surgical prophylaxis and shorten the duration of surgical prophylaxis in neurosurgery and general surgery. Changes of antibiotic choices for surgical prophylaxis in various clinics in 2014 and 2018 are summarized in Table 1. Appropriate surgical antibiotic prophylaxis duration times by surgical wards and by year of evaluation 2014 and 2018 are shown in Table 2.

**Table 1.** Surgical antibiotic prophylaxis – antimicrobial agent, change in years

Clinics -antibiotics	2014 n (%)	2018 n (%)	P
Obstetrics and gynecology			
Cefazolin	252 (91.6)	326 (87.2)	0.07
Others (mainly metronidazole combination)	23 (8.4)	48 (12.8)	
Neurosurgery			
Cefazolin	302 (93.2)	397 (100)	<0.01
Ceftriaxone	22 (7.8)	0	
General surgery			
Ampicillin sulbactam	108 (41.8)	389 (71.2)	<0.01
Cefazolin	23 (8.9)	95 (17.4)	
Ceftriaxone	127 (49.3)	62 (11.4)	
Urology			
Cefazolin	1 (1)	0	<0.01
Cefuroxime	83 (69)	128 (100)	
Ceftriaxone	36 (30)	0	
Orthopedics and traumatology			
Cefazolin	262 (100)	219 (100)	-
Ampicillin sulbactam*		194 (88.6)	

\*Prophylaxis continued with ampicillin sulbactam after cefazolin administration. \*\*% means column % in clinic subset.

**Table 2.** Surgical antibiotic prophylaxis surveillance-duration

Surveyed clinics	2014				2018				P
	Appropriate duration		Prolonged		Appropriate duration		Prolonged		
	n	%	n	%	n	%	n	%	
Obstetrics and gynecology	213	77.5	62	22.5	97	26	277	74	<0.01
Neurosurgery	151	46.6	173	53.4	392	98.7	5	1.3	<0.01
General surgery	107	41.5	151	58.5	296	54.2	250	45.8	<0.01
Orthopedics and traumatology	265	100	0	0	217	52.6	196	47.4	<0.01
Urology	36	30	84	70	4	3	124	97	<0.01
Hospital total surveyed clinics	772	62	470	38	1006	54.3	852	45.7	<0.01

Appropriate duration: Up to 72 h for orthopedic surgery, up to 24 h for others

## Antibiotic Usage

Antibiotic consumption for the ATC class J01 (i.e., antibacterial for systemic use) was 80.5 DDD per 100 patient days in 2014, and 64.8 DDD per 100 patient days in 2018. Table 3 shows the consumption of antimicrobials by ATC groups, expressed as DDD per 100 patient days, in all adult wards, including intensive care units in 2014 and 2018, April to July. The most used classes were penicillins without antipseudomonal activity combined with beta-lactamase inhibitors (J01CR01, J01CR02, and J01CR04), third-generation cephalosporins (J01DB), and first-generation cephalosporins (J01DC). We could achieve 45% reduction in third-generation cephalosporin consumption and 48% reduction in fluoroquinolone consumption. There were some increases in consumption of tetracyclines (J01AA), second-generation cephalosporins (J01DC), and glycopeptides (J01XA) but these were minor in terms of DDDs. Carbapenem and polymyxin use also decreased by 26% and 58%, respectively, but decrease in polymyxins may be related to temporary shortages in hospital pharmacy.

In surgical wards, antibiotic usage rate was 46.4% (111 of 239 inpatients) in 2014 PPS and 49.6% in 2018 PPS (121 of 244 inpatients) ( $p=0.49$ ). Approximately in half of the surgi-

cal patients treated with antibiotics, antibiotics were given inappropriately (49 of 111 patients in 2014 PPS; and 54 of 121 patients in 2018 PPS) ( $p=0.94$ ).

In medical wards, 64 of 216 inpatients were taking antibiotics on the day of 2014 PPS with the rate of 29.6%. Antibiotic usage rate decreased to 25.4% (47 in 185 inpatients) in 2018 PPS, ( $p=0.35$ ). Appropriateness was 79.7% (51 in 64 patients) and 87.2% (41 in 47 patients) in 2014 and 2018 PPS, respectively ( $p=0.29$ ).

In both 2014 and 2018 PPSs, more patients in surgical wards were taking antibiotics ( $p<0.01$ ) but appropriateness, in terms of compliance with guidelines was higher in medical wards ( $p<0.01$ ). There was no statistically significant change in antibiotic usage and appropriateness between 2014 and 2018 in both medical and surgical units.

In the PPS conducted in 2014 when the distribution of antibiotic use was evaluated in surgical clinics, it was seen that 66.7% ( $n=74$ ) of the patients had prophylaxis and 33.3% ( $n=37$ ) of them were treated with antibiotics. The most commonly used antibiotics for treatment in surgical clinics were cefazolin (44.1%;  $n=49$ ), ampicillin-sulbactam (19.8%;  $n=22$ ), and ceftriaxone (19.8%;  $n=22$ ), respectively. In the PPS conducted in 2018, the most commonly used antibi-

**Table 3.** Antibiotic consumption of all antibacterial for systemic use (J01) in adult wards, 2014 and 2018

Therapeutic group	2014		2018	
	DDD	DDD/100 pd	DDD	DDD/100 pd
Tetracyclines (J01AA)	112	0.3	445	1
Penicillins with extended spectrum(PES) (J01CA)	189	0.5	344	0.8
Beta-lactamase sensitive penicillins (J01CE)	227	0.6	222.5	0.5
PES without antipseudomonal activity+ beta-lactamase inhibitors (J01CR01, J01CR02, J01CR04)	10698	28.15	10337	24.5
Antipseudomonal penicillins+ beta-lactamase inhibitors (J01CR05)	931.7	2.5	821.4	1.9
First-generation cephalosporins (J01DB)	3643	9.6	3456	8.1
Second-generation cephalosporins (J01DC)	231.3	0.6	633.5	1.5
Third-generation cephalosporins (J01DD)	4756.8	12.52	2954.5	6.9
Fourth-generation cephalosporins (J01DE)	24.8	0.07	64.5	0.2
Carbapenems (J01DH)	2862.2	7.5	2361.8	5.5
Sulfamethoxazole and trimethoprim (J01EE01)	42	0.11	488.8	1.1
Macrolides, lincosamides, streptogramins (J01F)	771.3	2.01	936.8	2.2
Aminoglycosides (J01GB)	402.6	1.06	253.4	0.6
Fluoroquinolones (J01MA)	2797.2	7.36	1580.5	3.7
Glycopeptides (J01XA)	288.4	0.8	540.3	1.3
Polymyxins (J01XB)	551	1.45	264.5	0.6
Imidazole derivatives (J01XD)	1519	4	1370.8	3.2
Others	554.7	1.4	601	1.2
Antibiotics for systemic use (total J01)	30602	80.5	27319.4	64.8

DDD: Daily defined dose; pd: Patient day. 2014 pd: 37997 2018 pd: 42595

otics in surgical clinics were ampicillin-sulbactam (43%; n=55) and ceftazolin (39%; n=50).

When antibiotic appropriateness was evaluated in 2014, antibiotic usage in 35.4% (n=62/175) of medical and surgical patients was evaluated as "inappropriate." There were more than one reason for inappropriateness in 22 patients. In all patients receiving antibiotherapy, 10.2% (n=18) considered as unnecessary, 7.4% (n=13) as microbiologically inappropriate, 14.2% (n=25) as pharmacologically inappropriate, and finally as 16% (n=28) as prolonged surgical prophylaxis.

For out-patient antimicrobial stewardship, a total of 22.445 throat samples for RADT and throat culture were collected at the pediatric emergency clinic between November 2014 and April 2018. Bacterial tonsillopharyngitis were diagnosed in 24.9% (n=5591) of these patients and 75.1% (n=16854) of suspected cases have been treated without

antibiotics. We diagnosed 98.5% (n=5511) of GABHS in a short time such as 30 min with RADT and we applied antibiotherapy. In 2018–2019 influenza season, a total of 628 patients underwent IRAT for influenza-like symptoms. Influenza A or B positivity rates were 37.7% (n=237).

### Rifampicin

As a result of the cooperation with the related clinics and prepared guidelines, rifampicin ampoule consumption gradually decreased and discontinued within 1 year in local wound care. One hundred-eighty-nine rifampicin ampoules consumed in the quarter of 2014 (between April-June), whereas there were no consumption in 2018.

### Microbiology and Culture Sampling

Our local antimicrobial susceptibility profiles were prepared (Table 4). MRSA percentages for 2014–2017 range 13–28% for outpatient, 17–25% for inpatient, and 29–44%

**Table 4.** Local cumulative antimicrobial susceptibility profiles

Species	Antibiotic	Susceptibility percentages from 2014 to 2017 (%)		
		Out-patient	In-patient	ICU
Escherichia coli	CRO	74-75-73-72	70-58-57-55	46-48-58-58
	MEM	99-99-99-97	99-99-99-93	100-99-100-100
	CIP	76-77-73-72	69-65-63-59	55-55-79-63
	GN	85-87-85-84	82-78-77-73	73-74-82-80
	AK	99-99-99-97	99-99-98-92	100-99-99-96
Klebsiella pneumoniae	CRO	56-66-61-61	48-53-34-52	48-26-42-46
	MEM	94-95-97-92	97-88-83-90	94-69-72-79
	CIP	74-79-71-67	70-66-49-64	77-40-53-60
	GN	81-82-81-78	72-75-66-79	70-41-58-61
	AK	96-98-96-90	96-95-89-89	100-82-91-80
Pseudomonas aeruginosa	CAZ	80-83-88-87	92-84-83-89	NA
	PIP-TAZO	91-82-92-85	96-82-85-85	NA
	MEM	87-82-95-90	90-86-87-87	NA
	CIP	82-82-85-76	88-81-84-85	NA
	GN	81-79-89-84	85-81-88-89	NA
	AK	95-95-96-96	97-95-92-90	NA
Acinetobacter baumannii	MEM	NA	24-18-23-17	7-3-5-2
	CIP	NA	12-16-23-13	1-3-6-2
	GN	NA	23-18-30-23	14-6-7-6
	AK	NA	27-46-32-15	24-30-9-4
	TMP-SXT	NA	43-43-34-22	16-22-15-22
Staphylococcus aureus	CC	93-88-89-90	98-70-86-80	NA-72-81-67
	ER	86-82-85-89	89-69-82-80	NA-72-71-67
	LZD	98-99-100-100	100-99-100-100	NA-100-98-100
	TET	100-100-82-86	100-100-78-85	NA-100-64-63
	CIP	100-94-89-97	NA-94-90-97	NA-86-81-72

ICU: Intensive care unit; CRO: Ceftriaxone; MEM: Meropenem; CIP: Ciprofloxacin; GN: Gentamicin; AK: Amikacin; CAZ: Ceftazidime; PIP-TAZO: Piperacillin-Tazobactam; TMP-SXT: Trimethoprim-Sulfamethoxazole; CC: Clindamycin; ER: Erythromycin; LZD: Linezolid; TET: tetracycline; NA: non-applicable, number of Pseudomonas aeruginosa isolates for ICU and Acinetobacter baumannii isolates for out-patient were too low (n<30) to calculate susceptibility percentages.

for ICU. The PPS in 2014 showed that the rates of collecting blood and suspected site cultures were low before beginning of antibiotherapy (31.6%; n=60). These rates were 10.8% (n=12) in surgical clinics, 57.8% (n=37) in internal clinics and 73.3% (n=11) in ICUs. Microbiological sampling rate in surgical clinics was significantly lower than medical clinics and ICUs (p<0.05).

## Discussion

Turkey has the highest rate of antibiotic consumption among Organization for Economic Co-operation and Development countries. In 2013, the National Action Plan on Rational Drug Use was developed and implemented to reduce the rate of antibiotic consumption in Turkey.<sup>[19,20]</sup> In line with the National Action Plan, we have achieved positive developments after implementation of ASP in our hospital like other countries.<sup>[21,22]</sup> Italy and Turkey are both countries with high antimicrobial resistance rates. Barchitta et al. reported antibiotic consumption in Southern Italy for the ATC class J01 (i.e., antibacterial for systemic use) in hospitals to be in the range of 74.2–100.7 DDD per 100 patient days from 2015 to 2017. Our results show similar consumption in 2014 with 80.5 DDD per 100 patient days, while it was found to be reduced to 64.8 DDD/100 patient days in 2018.<sup>[23]</sup>

Studies have shown that approximately 30% of antibiotics used in hospitals are misused or unnecessary.<sup>[24]</sup> Antimicrobial resistance may occur due to inappropriate antibiotic use and ASP is shown to affect the use of appropriate antibiotics positively.<sup>[25,26]</sup> In a study conducted in China, the rate of antibiotic use was 39.4%, the most commonly used antibiotics were first-generation cephalosporins (19.9%) and ampicillin-sulbactam (19.1%). They found appropriate antibiotic use as 64.2%.<sup>[27]</sup> Similar results were obtained in a PPS conducted in our country that included 113 patients in 2018 (rate of antibiotic use was 70.8% and inappropriate antibiotic use was 33.8%).<sup>[28]</sup> When the data of our hospital were examined, antibiotic preferences and appropriate antibiotic usage rates of 65.8% (n=125) were also consistent with the literature.

The aim of surgical prophylaxis is to prevent contamination in clean-contaminated and some clean operations until the incision is closed. Studies and published guidelines suggest that prophylaxis should be administered within 60 min before the first incision to keep the time minimum between prophylaxis and surgery onset.<sup>[29]</sup> ASP is important for optimizing surgical antibiotic prophylaxis duration times. Saied et al. evaluated five surgical hospitals in a before-and-after intervention study. This multicenter pilot intervention study shows that all hospitals showed a significant rise in the optimal duration of surgical prophylaxis

after implementation of ASP.<sup>[30]</sup> van Kasteren et al. audited the quality of prophylaxis before and after the intervention. They found that prolonged prophylaxis was only in 31.4% cases instead of 46.8% expected cases in 13 Dutch hospitals.<sup>[31]</sup> It should be considered that unnecessary prolonged prophylaxis leads to increased cost, infection with resistant bacteria, and undesirable side effects. When we examined our surgical clinics, we could achieve right administration time after implementing ASP in our hospital. We reduced the use of broad spectrum antibiotics, but could not limit the prolonged use of surgical prophylaxis except neurosurgical and general surgery operations.

As our enterobacteriaceae resistance rates to cefazolin and ampicillin sulbactam were similar, we offered ampicillin sulbactam as an alternative in biliary surgery. World Health organization (WHO) experts are also recommending cefazolin, cefuroxime, and amoxicillin clavulanic acid as first-line prophylactic agents for cholecystectomy in "The Selection and Use of Essential Medicines Report of the 22<sup>nd</sup> WHO Expert Committee."<sup>[32]</sup> It is also stated in the report that there is no reason to use ceftriaxone for surgical prophylaxis agent as it belongs to the Essential Medicine List-Watch group and WHO highest-priority, critically important antimicrobials list.<sup>[33,34]</sup>

Ceftriaxone does not have additional effect on extended spectrum beta-lactamase producing bacteria and has high risk of selecting resistant bacteria. In a multidisciplinary meeting that we invited Urology Clinic to our ACT about the excessive ceftriaxone use, clinicians stated their concerns to use cefazolin as prophylaxis because of its weak effectiveness on Gram-negative agents and a decision of using a second-generation cephalosporin as first-line prophylactic agent for clean-contaminated urologic surgery has been taken. In our results, it's seen that ceftriaxone use is avoided to be used for urologic surgery and cefuroxime has taken its place. Cefuroxime is also recommended as a first choice agent for urologic surgeries by the WHO expert committee.<sup>[32]</sup> Sharma et al. found that surgical prophylaxis protocol with one dose cefuroxime was effective in 89.5% of patients who underwent clean or clean-contaminated urologic surgery.<sup>[35]</sup>

Local cumulative antibiograms are very important for antibiotic stewardship at local level. Physicians' prior knowledge of local drug resistance rates will support their clinical decision-making and guide the empirical treatment choices. Furthermore, changes about local cumulative antimicrobial susceptibility profiles uncover resistance over time and drug-resistant organisms.<sup>[36-38]</sup> Based on the importance of publishing local antibiograms, we have regularly edited our annual local antibiogram data since 2013.

Upper respiratory tract infections are the most common causes of excessive antibiotic use among outpatients. Diagnosis of bacterial tonsillopharyngitis should be confirmed by laboratory tests in patients whose signs and symptoms support bacterial etiology. Throat culture is the gold standard method for the diagnosis of bacterial tonsillopharyngitis and RADT is a high-sensitive, quick, cost-effective, and reliable tool for screening bacterial tonsillopharyngitis. As waiting culture results may lead to delay in treatment or may cause antibiotic prescription without evaluation of culture results, we used RADT in addition to throat culture to guide our treatment plan and to take early results.<sup>[39,40]</sup>

This study had some limitations. First, due to the changes made in the digitalization stages of our hospital system, data before 2014 could not be reached. Second, we did not have any data on antibiotic prescribing rates before the use of RADT in patients with acute tonsillopharyngitis. Third, we could not analyze any changes about culture sampling rates after implementation of ASP because this data were not analyzed in the PPS conducted in 2018. Fourth, there are no clinical outcomes (i.e., effects on mortality or on clostridium difficile infection incidence) or effects on antibiotic susceptibility profile reported after ASP implementation, only process measures used. Fifth, cost-effectiveness has not been investigated in the studies conducted with ASP in our hospital.

## Conclusion

This is one of the first comprehensive studies carried out in accordance with CDC recommendations generated by the ASP for a hospital in Turkey. In this global antimicrobial resistance era, all hospitals should have motivated antimicrobial stewardship teams, determine the low hanging fruits for their institutions and give feedbacks to the prescribing clinicians about their surveillance. Improvement in rational antibiotic use is hard to achieve without multidisciplinary involvement, especially surgeons.

## Disclosures

**Ethics Committee Approval:** The study was assessed by the Regional Ethical Review Board in Sisli, Turkey on 16<sup>th</sup> April 2019, registration number 2347.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

**Authorship Contributions:** Concept – N.D., E.A.; Design – N.D., E.E.A., A.O.; Supervision – N.D., B.B., C.A.; Materials – N/A; Data collection &/or processing – N.D., E.E.A., C.A., A.O.; Analysis and/or interpretation – E.E.A., N.D., A.O., B.B.; Literature search – E.E.A., N.D., E.A.; Writing – E.E.A., N.D., A.O.; Critical review – N.D., E.A., B.B., C.A.

## References

1. Dellit TH. Summary of the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for developing an institutional program to enhance antimicrobial stewardship. *Infect Dis Clin Pract* 2007;15:263–4. [CrossRef]
2. Perozziello A, Routelous C, Charani E, Truel A, Birgand G, Yazdapanah Y, et al; CEFECA Study Group. Experiences and perspectives of implementing antimicrobial stewardship in five French hospitals: a qualitative study. *Int J Antimicrob Agents* 2018;51:829–35.
3. McGowan JE Jr, Gerding DN. Does antibiotic restriction prevent resistance? *New Horiz* 1996;4:370–6.
4. Dyar OJ, Huttner B, Schouten J, Pulcini C; ESGAP (ESCMID Study Group for Antimicrobial stewardship). What is antimicrobial stewardship? *Clin Microbiol Infect* 2017;23:793–8. [CrossRef]
5. Pulcini C, Binda F, Lamkang AS, Trett A, Charani E, Goff DA, et al. Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach. *Clin Microbiol Infect* 2019;25:20–5. [CrossRef]
6. Lee KB, Ramirez JA, Collins R, Bucheit J, Sanogo K, Stevens MP. Antimicrobial stewardship practices in Virginia. *Am J Infect Control* 2017;45:451–2. [CrossRef]
7. Richards DA, Hanson J. Successful antimicrobial stewardship program collaboration. *Am J Infect Control* 2017;45:19. [CrossRef]
8. Centers for Disease Control and Prevention. Checklist for Core Elements of Hospital Antibiotic Stewardship Programs. Available at: <https://www.cdc.gov/antibiotic-use/healthcare/pdfs/checklist.pdf>. Accessed May 10, 2019.
9. Leaper DJ, Edmiston CE. World Health Organization: global guidelines for the prevention of surgical site infection. *J Hosp Infect* 2017;95:135–6. [CrossRef]
10. Graft-Aikins A, Chalker J, Lee D, Miralles M. Interventions and strategies to improve the use of antimicrobials in developing countries: A review. Available at: <https://www.who.int/csr/resources/publications/drugresist/Interventions.pdf>. Accessed Apr 5, 2021.
11. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, 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. [CrossRef]
12. Özlü T, Bülbül L, Alataş F, Arseven O, Şakar Coşkun A, Çilli A et al. Diagnosis and Treatment Consensus Report of Community-Acquired Pneumonia in Adults. *Turk Thorac J* 2009;10:3–16.
13. World Health Organization (WHO). ATC/DDD Index. Available at: [https://www.whocc.no/atc\\_ddd\\_index](https://www.whocc.no/atc_ddd_index). Accessed May 10, 2019.
14. Harnden A, Perera R, Brueggemann AB, Mayon-White R, Crook DW, Thomson A, et al. Respiratory infections for which general practitioners consider prescribing an antibiotic: a prospective study. *Arch Dis Child* 2007;92:594–7. [CrossRef]



15. Shlomo V, Adi R, Eliezer K. The knowledge and expectations of parents about the role of antibiotic treatment in upper respiratory tract infection—a survey among parents attending the primary physician with their sick child. *BMC Fam Pract* 2003;4:20. [CrossRef]
16. Zyoud SH, Abu Taha A, Araj KF, Abahri IA, Sawalha AF, Sweileh WM, et al. Parental knowledge, attitudes and practices regarding antibiotic use for acute upper respiratory tract infections in children: a cross-sectional study in Palestine. *BMC Pediatr* 2015;15:176.
17. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 infectious diseases society of america clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *J Am Podiatr Med Assoc* 2013;103:2–7. [CrossRef]
18. CLSI. Analysis and presentation of cumulative antimicrobial susceptibility test data; approved guideline—4th Edition. CLSI document M39-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
19. Versporten A, Bolokhovets G, Ghazaryan L, Abilova V, Pyshnik G, Spasojevic T, et al; WHO/Europe-ESAC Project Group. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. *Lancet Infect Dis* 2014;14:381–7. [CrossRef]
20. Aksoy M, Alkan A, Isli F. Rational Drug Use Promotional Activities of Ministry of Health. *Turkiye Klinikleri J Pharmacol-Special Topics* 2015;3:19–26.
21. Skoog G, Struwe J, Cars O, Hanberger H, Odenholt I, Prag M, Skär-lund K, Ulleryd P, Erntell M. Repeated nationwide point-prevalence surveys of antimicrobial use in Swedish hospitals: data for actions 2003–2010. *Euro Surveill* 2016;21. [CrossRef]
22. Muraki Y, Yagi T, Tsuji Y, Nishimura N, Tanabe M, Niwa T, et al. Japanese antimicrobial consumption surveillance: First report on oral and parenteral antimicrobial consumption in Japan (2009–2013). *J Glob Antimicrob Resist* 2016;7:19–23. [CrossRef]
23. Barchitta M, Quattrocchi A, Maugeri A, La Rosa MC, La Mastra C, Sessa L, et al. Antibiotic Consumption and Resistance during a 3-Year Period in Sicily, Southern Italy. *Int J Environ Res Public Health* 2019;16:2253. [CrossRef]
24. Centers for Disease Control and Prevention. Antibiotic use in the United States, 2017: Progress and Opportunities. Available at: <https://www.cdc.gov/antibiotic-use/stewardship-report/pdf/stewardship-report.pdf>. Accessed May 7, 2019.
25. Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review. *Antimicrob Resist Infect Control* 2019;8:35. [CrossRef]
26. Madran B, Keske Ş, Tokça G, Dönmez E, Ferhanoglu B, Çetiner M, et al. Implementation of an antimicrobial stewardship program for patients with febrile neutropenia. *Am J Infect Control* 2018;46:420–4. [CrossRef]
27. Qu X, Yin C, Sun X, Huang S, Li C, Dong P, et al. Consumption of antibiotics in Chinese public general tertiary hospitals (2011–2014): Trends, pattern changes and regional differences. *PLoS One* 2018;13:e0196668. [CrossRef]
28. Ergül AB, Gökçek İ, Çelik T, Torun YA. Assessment of inappropriate antibiotic use in pediatric patients: Point-prevalence study. *Turk Pediatri Ars* 2018;53:17–23. [CrossRef]
29. Tarchini G, Liau KH, Solomkin JS. Antimicrobial stewardship in surgery: challenges and opportunities. *Clin Infect Dis* 2017;64:S112–4.
30. Saied T, Hafez SF, Kandeel A, El-kholy A, Ismail G, Aboushady M, et al. Antimicrobial stewardship to optimize the use of antimicrobials for surgical prophylaxis in Egypt: A multicenter pilot intervention study. *Am J Infect Control* 2015;43:e67–71. [CrossRef]
31. van Kasteren ME, Mannien J, Kullberg BJ, de Boer AS, Nagelkerke NJ, Ridderhof M, et al. Quality improvement of surgical prophylaxis in Dutch hospitals: evaluation of a multi-site intervention by time series analysis. *J Antimicrob Chemother* 2005;56:1094–102.
32. World Health Organization (WHO). The selection and use of essential medicines. WHO Technical Report Series 2019. Available at: [https://www.who.int/medicines/publications/essentialmedicines/UNEDITED\\_TRS\\_2019\\_EC22\\_Sept.pdf?ua=1](https://www.who.int/medicines/publications/essentialmedicines/UNEDITED_TRS_2019_EC22_Sept.pdf?ua=1). Accessed Apr 6, 2021.
33. World Health Organization (WHO). WHO model list of essential medicines, 20th list. Geneva: World Health Organization; 2017. Available at: <https://www.who.int/medicines/publications/essentialmedicines/en/>. Accessed Jan 15, 2019.
34. World Health Organization (WHO). Critically important antimicrobials for human medicine, 5th revision. Available at: <https://www.who.int/foodsafety/publications/antimicrobials-fifth/en/>. Accessed Apr 6, 2021.
35. Sharma AP, Devana SK, Bora GS, Mavuduru RS, Mohan B, Taneja N, et al. Protocol-based perioperative antimicrobial prophylaxis in urologic surgeries: Feasibility and lessons learned. *Indian J Urol* 2019;35:141–6.
36. Gül M, Seber E. The distribution of the microorganisms that have been isolated from wound and abscesses in consideration of clinics and their antibiotic susceptibility. *Sisli Etfal Hastan Tip Bul* 2002;36:13–8.
37. Hindler JF, Stelling J. Analysis and presentation of cumulative antibiograms: a new consensus guideline from the Clinical and Laboratory Standards Institute. *Clin Infect Dis* 2007;44:867–73.
38. Bayraktar B, Pelit S, Bulut ME, Aktaş E. Trend in antibiotic resistance of extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* bloodstream infections. *Sisli Etfal Hastan Tip Bul* 2019;53:70–5. [CrossRef]
39. Ekşi Alp E, Dalgıç N, Kına N, Bayraktar B, Öncül A, Aktaş Sepetci E. The importance of rapid antigen testing for group A streptococcal tonsillopharyngitis: A single center experience. *J Pediatr Inf* 2018;12:93–8. [CrossRef]
40. Hersh AL, Jackson MA, Hicks LA; American Academy of Pediatrics Committee on Infectious Diseases. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics* 2013;132:1146–54. [CrossRef]