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ORIGINAL ARTICLE

Assessment of antibiotic prescribing at different hospitals and primary health care facilities

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Abstract In this study, it was aimed to investigate the utilization of antibiotics at various health care facilities. Photocopies of 1250 prescriptions which were containing antibiotics and written out in primary health care facilities (PHCFs), public hospitals (PHs), private hospitals and university hospitals in 10 provinces across Turkey, were evaluated by some drug use indicators. The number of drugs per prescription was 3.23 ± 0.92 and it was highest in PHCFs (3.34 ± 0.84), ($p < 0.05$). The cost per prescription was 33.3 $, being highest in PHs while being lowest in PHCFs (38.6 $ and 28.2 $ respectively). Antibiotic cost per prescription was 16.7 $ and it was also highest and lowest in PHs and PHCFs respectively ($p < 0.05$). The most commonly prescribed group of antibiotics was "beta-lactam antibacterials, penicillins" (29.2%) while amoxicillin/clavulanic acid was the most commonly prescribed antibiotic (18.1%). Sixty-one percent of the antibiotics prescribed for acute infections was generics; among facilities being highest in PHCFs (66.5%) and among diagnosis being highest in acute pharyngitis. In general, the duration of antibiotic therapy was approximately 7 days for acute infections. Although much more drugs were prescribed in PHCFs than others, it was found to be in an inverse proportion with both the total cost of prescriptions and the cost of antibiotics. Broad-spectrum antibiotics, beta-lactamase combinations in particular, were considered to be more preferable in all health care facilities is also notable. These results do serve as a guide to achieve the rational use of antibiotics on the basis of health care facilities and indications.

1. Introduction

Antibiotics are the agents which are commonly used in the treatment of bacterial infections. In spite of their advantages in treatment, the problems that occur from the irrational use of antibiotics (IUA) have put them in the health agendas of the countries as a common issue of consideration (Holloway and van Dijk, 2011; WHO, 2001; European Parliament

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Directorate General for Internal Policies of the Union, 2006; Gould and van der Meer, 2005). The use of antibiotics for viral infections, unnecessarily prescribing broad-spectrums, use of inappropriate doses and durations, patients' self-treatments, etc. can be given as the examples of IUA which lead to antibiotic resistance, ineffective treatment and increased health expenditures (WHO, 2001; European Parliament Directorate General for Internal Policies of the Union, 2006; Ochoa et al., 2000; Llor et al., 2009; Colgan and Powers, 2001).

Countries have taken some initiatives at national and international levels in order to promote the rational use of antibiotics (WHO, 2001; Gould and van der Meer, 2005; Shah and Shah, 2008; Mölstad and Cars, 1999; Goossens et al., 2006). In spite of these initiatives, IUA still remains as a problem which can be caused by physicians or many other factors such as patients, physical working environments of medical practice, etc. (Colgan and Powers, 2001; Kotwani et al., 2010; Niederman, 2005; Ozgenç et al., 2011). Physicians are the health professionals who are primarily responsible for treatment and to know about their prescribing practices can contribute to the achievement of initiatives and regulations relevant to IUA (WHO, 2002, 2003; Natsch, 2005). With the "Health Transformation Program" launched in 2003, the Turkish Ministry of Health (MoH) identified a number of strategies aiming to prevent the irrational use of drugs in Turkey. Conducting field surveys and providing scientific evidences are among these strategies (Akdağ, 2011). Most of the studies examining the prescribing attitudes of physicians in the literature are usually, specific to a particular health care facility, a region, an indication or an age group (Aydın et al., 2005; Lundborg et al., 2002; Pathak et al., 2011; Akici et al., 2004; Rossignoli et al., 2007; Ceyhan et al., 2010; Bjerrum et al., 2004; Baktygul et al., 2011; Peláez-Ballestas et al., 2003; Avci et al., 2006; Sharma et al., 2009; Kumar et al., 2010; Vojvodić, 2010; Vaccheri et al., 2002). Nonetheless, it is needed to carry out comprehensive researches that make an assessment of the use of antibiotics by various health care facilities. In this study, it was aimed to analyze the contents of the antibiotic prescribed scripts which were written out in various health care facilities in various provinces across Turkey.

2. Material and methods

A comprehensive study assessing the prescriptions from various health care facilities was carried out in 2009 under the responsibility of the School of Public Health (TUSAK), with the permission given by Turkish MoH. In this manuscript, only antibiotic containing prescriptions which were collected within the scope of this study were analyzed. Photocopies of the prescriptions, which were written out in the primary health care facilities (PHCFs), public hospitals (PHs), private hospitals (PTE-Hs) and university hospitals (UHs) in November–December 2009, were collected by randomization during the patients' visits to the pharmacies. Of these prescriptions, a total of 1250 prescriptions containing antibiotics were analyzed retrospectively in this study.

Turkey has 81 provinces and the population was 72.561.312 as of 2009 (Turkish Statistical Institute, 2011). In this cross-sectional study, the prescriptions containing antibiotics, which were written out in PHCFs, PHs, PTE-Hs and UHs running in 10 provinces (Eskisehir, Denizli, Nigde, Nevsehir, Bartin, Karabuk, Gumushane, Bayburt, Cankiri and Kirsehir) that are located in various geographical regions of Turkey, were assessed in detail by drug utilization indicators. Data were collected by a member of the survey team and a health care professional who was practicing in that province. The prescriptions written out in PHCFs and PHs were collected in all of 10 provinces where the survey was conducted. The prescriptions written out in UHs were collected in Denizli and Eskisehir provinces since they have medical schools; except Gumushane and Bayburt provinces, since no private hospitals were available, the prescriptions written out in PTE-Hs were collected in all provinces. The provinces were selected randomly and in order to avoid from any bias, utmost significance was attached to selecting provinces where no pilot study was conducted before for the purpose of rational use of drugs (RUD).

The prescriptions were computerized into the databases that were specifically developed with the Excel and SPSS. They were assessed for number of drugs per prescription (NDPP), number of antibiotics per prescription (NAPP), cost per prescription (CPP), antibiotic cost per prescription (ACPP), main groups of all drugs written on the prescriptions, groups of antibiotics, the most frequently prescribed antibiotics, etc.

Some of the prescriptions included more than one diagnosis. Among the prescriptions, the ones with a diagnosis of a single infection ($n = 951$) were analyzed in detail in another study (Mollahaliloğlu et al., 2012). In the present study, among single-diagnosis prescriptions which were indicated "acute" ($n = 343$) were assessed in terms of the "average duration of antibiotic therapy" and "generic or original antibiotic prescribing". These assessments were also specifically reviewed for the most common first four indications. The antibiotic groups and generic antibiotics, which were preferred for these top four indications, were specifically examined for "acute indications". The information regarding the duration of antibiotic therapy was not available in the prescriptions. Therefore, the duration of antibiotic therapy was determined by prescribed total amount and instructions of antibiotics for acute indications. While considering the average duration of antibiotic therapy, the prescriptions, which did not indicate doses, and the pharmaceutical forms, which can be used externally, were not included in order to obtain quantitative data.

ANOVA, Tukey Hsd, Kruskal Wallis and Chi-Square tests were used in the statistical analyses. The comparisons were considered as statistically significant, if $p < 0.05$. Drugs were grouped by the ATC (Anatomic Therapeutic Chemical) classification. While calculating the prices of drugs, the values established by MoH at the date of data collection were taken into consideration. In this study, these prices were given in the US Dollars ($) by the foreign exchange rate that was effective on the date of the survey.

3. Results

In this study, 1250 prescriptions, which were written out by 535 physicians practicing in various health care facilities (including PHCFs, PHs, PTE-Hs and UHs) in 10 provinces were analyzed (prescription per physician $n = 2.3$). Of the 1250 prescriptions, 423 (33.8%) were written out in PHCFs, 382 in PTE-Hs (30.6%), 371 in PHs (29.7%) and 74 (5.9%) in UHs. The mean age of the patients was 35.68 ± 23.41

and more than half of them were female (56.8%). Most of the prescriptions were written out by male physicians (70.5%).

The prescriptions containing antibiotics were written mostly by general practitioners (GPs), (33.8%), followed by specialists in pediatrics (12.2%), otolaryngology (11.5%), chest diseases (7.4%) and internal medicine (7.0%), (Fig. 1). In general, 33.8% of the prescriptions were written out by GPs, 34.9% by surgical medicine specialists and 31.3% by internal medicine specialists.

Some of the prescriptions included more than one diagnoses (number of diagnosis per prescription = 1.7). A total of 2057 diagnoses were written and pharyngitis (12.5%) was the most common followed by bronchitis (8.4%), sinusitis (7.9%) and tonsillitis (7.5%). The rank was also found to be the same in the distribution of the ''acute'' infectious diagnosis (Table 1).

Nearly half of the prescriptions (49.1%; $n = 614$) included analgesics, 10.6% ($n = 132$) of any injectable drugs and 7.8% ($n = 98$) of injectable antibiotics. Within the injectable drug prescribed scripts, three-fourth of them (74.2%) included injectable antibiotics.

A total of 4038 medicines were prescribed. NDPP was 3.23 ± 0.92 and it was highest in PHCFs (3.34 ± 0.84) and lowest in PHs (3.12 ± 1.00). NDPP by health care facilities showed statistically significant differences which were related to the higher NDPP in PHCFs than PHs ($p < 0.05$). Of the 4038 medicines, 34.8% ($n = 1403$) was antibiotics. NAPP was 1.12 ± 0.35, being highest in PTE-Hs (1.21 ± 0.44) and lowest in PHCFs (1.04 ± 0.19). NAPP by health care facilities showed statistically significant differences ($p < 0.05$). These differences were between PHCFs and all other facilities, and between PHs and PTE-Hs (Table 2). Of 1403 antibiotics, 7.3% ($n = 103$) was injectable.

The total cost of all prescribed medicines was 41655,36 $. The CPP was 33.32 ± 33.50 $, being highest in PHs (38.62 ± 46.57 $) and lowest in PHCFs (28.23 ± 19.62 $). CPP by health care facilities showed statistically significant differences. The CPP was higher in PHs than PHCFs ($p < 0.05$). The ACPP was 16.73 ± 13.62 $, being highest in PHs and PTE-Hs (17.87 ± 15.68 $ and 17.71 ± 14.31 $, respectively) and lowest in PHCFs (15.08 ± 11.42 $). ACPP by health care facilities showed statistically significant differences. The ACPP was lower in PHCFs than PHs and PTE-Hs ($p < 0.05$), (Table 2). The cost of antibiotics was 20917,68 $, which constituted 50.2% of the total cost of all the drugs prescribed. The cost of injectable antibiotics was 2577,19 $, which constituted 12.3% of the total antibiotic cost.

''Systemic anti-infectives'' (ATC code: J; 31.3%) was the most commonly prescribed drug group on prescriptions, followed by ''respiratory system medicines'' (R; 26.6%) and ''musculo-skeletal system medicines'' (M; 10.6%). Except PHCFs, ''systemic anti-infectives'' were found to be the most frequently prescribed drug group in the health care facilities and in PHCFs, it was ''respiratory system medicines (R)'', (Table 3).

When the ATC group distributions of all antibiotics were analyzed, ''beta-lactam antibacterials, penicillins'' (ATC code: J01C; 29.2%) were the most frequently prescribed antibiotics followed by ''other beta-lactam antibacterials'' (J01D; 28.0%), ''quinolone antibacterials (J01M; 15.8%)'' and ''macrolides, lincosamides and streptogramins'' (J01F; 8.9%)''. In PHCFs and UHs, ''beta-lactam antibacterials, penicillins'' (39.5% and 34.1%, respectively)'' were the most frequently prescribed antibiotics while in PHs and PTE-Hs, it was ''other beta-lactam antibacterials'' (26.9% and 27.8%, respectively)'', (Table 4).

Amoxicillin + clavulanic acid (18.1%) was the most prescribed antibiotic followed by cefuroxime (9.5%), ciprofloxacin (4.7%), moxifloxacin (4.7%) and levofloxacin (4.6%). Amoxicillin + clavulanic acid was found also to be the most prescribed antibiotic in all health care facilities. The second most frequently prescribed antibiotic had a similar trend and was found to be cefuroxime in all health care facilities (Table 5).

Of the total 1250 prescriptions, 951 had one diagnosis (76.1%). Among these one-diagnosed prescriptions, those indicated as acute (A.), ($n = 343$) were subjected to additional analyses (Table 1). The groups of antibiotics prescribed for

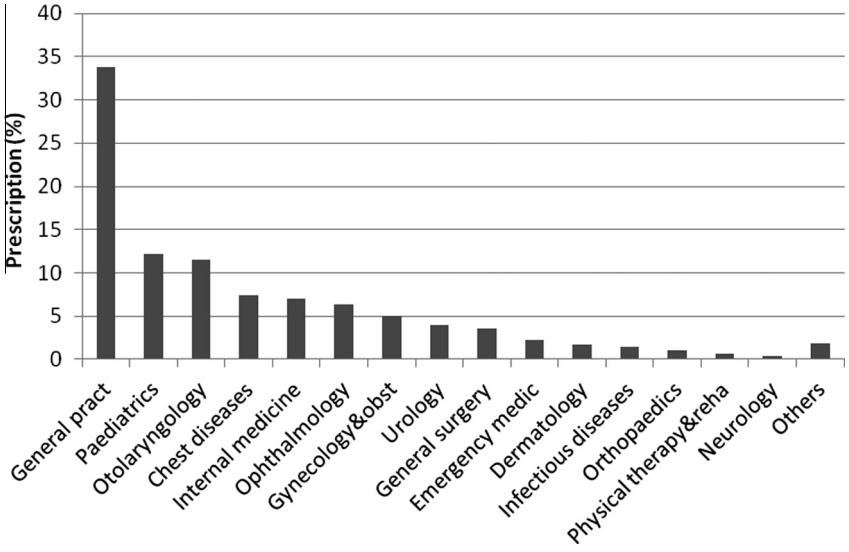

Figure 1 Distribution of the prescriptions by physicians' specialties.

Table 1 Distribution of the most commonly written diagnoses on prescriptions (*, percentage by 1250 prescriptions).

Diagnoses	Diagnoses on prescriptions			Diagnoses on prescriptions which were stated as "acute" infections		
	n	%	%*	*n*	%	%*
Pharyngitis	258	12.5	20.6	106	30.9	8.5
Bronchitis	173	8.4	13.8	90	26.2	7.2
Sinusitis	163	7.9	13.0	57	16.6	4.6
Tonsillitis	155	7.5	12.4	58	16.9	4.7
Others	1308	63.6	104.6	32	9.3	2.6
Total	2057	100.0	–	343	100.0	27.4

Table 2 Distribution of the average number of drugs per prescription (NDPP), average cost per prescription (CPP), average number of antibiotics per prescription (NAPP) and average antibiotic cost per prescription (ACPP) by healthcare facilities.

Healthcare facilities (n = Total number of prescriptions)	NDPP ± SD (n = Total number of drugs)	CPP ± SD ($)	NAPP ± SD (n = Total number of antibiotics)	ACPP ± SD ($)
PHCF (n = 423)	3.34 ± 0.84 (n = 1411)	28.23 ± 19.62	1.04 ± 0.19 (n = 438)	15.08 ± 11.42
PH (n = 371)	3.12 ± 1.00 (n = 1157)	38.62 ± 46.57	1.12 ± 0.35 (n = 416)	17.87 ± 15.68
PTE-H (n = 382)	3.22 ± 0.94 (n = 1230)	33.89 ± 30.38	1.21 ± 0.44 (n = 461)	17.71 ± 14.31
UH (n = 74)	3.24 ± 0.89 (n = 240)	32.95 ± 29.49	1.19 ± 0.43 (n = 88)	15.46 ± 8.63
Total (n = 1250)	3.23 ± 0.92 (n = 4038)	33.32 ± 33.50	1.12 ± 0.35 (n = 1403)	16.73 ± 13.62
Statistics	F = 3.682	F = 6.465	F = 17.535	F = 3.854
	p = 0.012	p = 0.000	p = 0.000	p = 0.009

Table 3 Distribution of the ATC classification of all the prescribed medicines by healthcare facilities.

ATC classification	PHCF		PH		PTE-H		UH		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Alimentary tract and metabolism (A)	154	10.9	94	8.1	114	9.3	25	10.4	387	9.6
Blood and blood forming organs (B)	8	0.6	15	1.3	14	1.1	4	1.7	41	1.0
Cardiovascular system (C)	32	2.3	9	0.8	12	1.0	4	1.7	57	1.4
Dermatologicals (D)	42	3.0	40	3.5	30	2.4	10	4.2	122	3.0
Genito urinary system and sex hormones (G)	5	0.4	21	1.8	22	1.8	3	1.3	51	1.3
Systemic hormonal prep. excluding sex hormones (H)	2	0.1	5	0.4	8	0.7	–	–	15	0.4
General antiinfectives for systemic use (J)	419	29.7	367	31.7	398	32.4	79	32.9	1263	31.3
Antineoplastic and immunomodulating agents (L)	–	–	1	0.1	2	0.2	–	–	3	0.1
Musculo-skeletal system (M)	171	12.1	106	9.2	123	10.0	27	11.3	427	10.6
Nervous system (N)	114	8.1	85	7.3	89	7.2	21	8.8	309	7.7
Antiparasitic products (P)	7	0.5	11	1.0	9	0.7	6	2.5	33	0.8
Respiratory system (R)	444	31.5	316	27.3	271	22.0	45	18.8	1076	26.6
Sensory organs (S)	11	0.8	85	7.3	137	11.1	16	6.7	249	6.2
Various (V)	2	0.1	2	0.2	1	0.1	–	–	5	0.1

the first four A. infections were examined in detail. Accordingly, for A. pharyngitis, "beta-lactam antibacterials, penicillins" (J01C; 46.3%)" and "other beta-lactam antibacterials" (J01D; 34.3%); for A. bronchitis, "other beta-lactam antibacterials (J01D; 33.7%) and "quinolone antibacterials" (J01M; 27.4%); for A. sinusitis, "other beta-lactam antibacterials" (J01D; 36.2%) and "beta-lactam antibacterials, penicillins" (J01C; 34.5%); for A. tonsillitis, "beta-lactam antibacterials, penicillins" (J01C; 66.7%) and "other beta-lactam antibacterials (J01D; 26.7%) were the most frequently prescribed groups of antibiotics (Table 6).

The most frequently prescribed antibiotics were analyzed for the most common A. infectious diseases. Accordingly, for A. pharyngitis amoxicillin + clavulanic acid (29.6%), cefuroxime (9.3%) and cefaclor (6.5%); for A. bronchitis cefuroxime (15.8%), amoxicillin + clavulanic acid (11.6%) and clarithromycin (10.5%); for A. sinusitis amoxicillin + clavulanic acid (27.6%) and with the same percentage (6.9%) cefuroxime, cefaclor and cefixime; for A. tonsillitis amoxicillin + clavulanic acid (46.7%), cefuroxime (10.0%) and combinations (6.7%) were the most frequently prescribed antibiotics (Table 7).

For A. infections, giving a consideration to the quantity of drugs prescribed and the recommended daily doses, the durations of antibiotic therapy were also examined. Accordingly, the average duration of antibiotic therapy was 6.83 ± 2.52 days (min: 1, max: 20 days) for A. infections.

Table 4 Distribution of the ATC 4 classification of antibiotics by healthcare facilities.

ATC classification	PHCF		PH		PTE-H		UH		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Beta-lactam antibacterials, penicillins (J01C)	173	39.5	100	24.0	107	23.2	30	34.1	410	29.2
Other beta-lactam antibacterials (J01D)	137	31.3	112	26.9	128	27.8	16	18.2	393	28.0
Quinolone antibacterials (J01M)	33	7.5	82	19.7	88	19.1	19	21.6	222	15.8
Macrolides, lincosamides and streptogramins (J01F)	55	12.6	32	7.7	32	6.9	6	6.8	125	8.9
Anti-infectives (S01A)	6	1.4	37	8.9	51	11.1	5	5.7	99	7.1
Other antibacterials (J01X)	11	2.5	19	4.6	16	3.5	4	4.5	50	3.6
Anti-inflammatory agents and anti-infectives in combination (S01C)	2	0.5	8	1.9	19	4.1	2	2.3	31	2.2
Antibiotics for topical use (D06A)	8	1.8	9	2.2	7	1.5	3	3.4	27	1.9
Tetracyclines (J01A)	3	0.7	11	2.6	2	0.4	2	2.3	18	1.3
Sulfonamides and trimethoprim (J01E)	5	1.1	–	–	6	1.3	–	–	11	0.8
Anti-acne preparations for topical use (D10A)	1	0.2	2	0.5	1	0.2	1	1.1	5	0.4
Intestinal antiinfectives (A07A)	2	0.5	2	0.5	–	–	–	–	4	0.3
Aminoglycoside antibacterials (J01G)	–	–	–	–	3	0.7	–	–	3	0.2
Chemotherapeutics for topical use (D06B)	2	0.5	–	–	–	–	–	–	2	0.1
Amphenicols (J01B)	–	–	1	0.2	1	0.2	–	–	2	0.1
Corticosteroids, combinations with antibiotics (D07C)	–	–	1	0.2	–	–	–	–	1	0.1
Total	438	100.0	416	100.0	461	100.0	88	100.0	1403	100.0

Table 5 Distribution of the most commonly prescribed ten antibiotics by healthcare facilities.

Antibiotic (ATC 5 Code)	PHCF (*n* = 438)		PH (*n* = 416)		PTE-H (*n* = 461)		UH (*n* = 88)		Total (*n* = 1403)	
n = Total number of antibiotics	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Amoxicillin + clavulanic acid (J01CR02)	115	26.3	69	16.6	46	10.0	24	27.3	254	18.1
Cefuroxime (J01DC02)	43	9.8	45	10.8	38	8.2	7	8.0	133	9.5
Ciprofloxacin (J01MA02)	–	–	29	7.0	26	5.6	6	6.8	66	4.7
Moxifloxacin (J01MA14)	11	2.5	21	5.0	28	6.1	6	6.8	66	4.7
Levofloxacin (J01MA12)	11	2.5	20	4.8	27	5.9	6	6.8	64	4.6
Clarithromycin (J01FA09)	24	5.5	14	3.4	17	3.7	6	6.8	61	4.3
Cefaclor (J01DC04)	22	5.0	12	2.9	17	3.7	–	–	52	3.7
Sultamicillin (J01CR04)	12	2.7	–	–	26	5.6	2	2.3	51	3.6
Cefpodoxime (J01DD13)	15	3.4	13	3.1	16	3.5	6	6.8	50	3.6
Amoxicillin (J01CA04)	21	4.8	–	–	–	–	–	–	36	2.6
Cefprozil (J01DC10)	14	3.2	–	–	–	–	–	–	–	–
Cefditoren (J01DD16)	–	–	12	2.9	–	–	–	–	–	–
Gemifloxacin (J01MA15)	–	–	12	2.9	–	–	–	–	–	–
Ceftriaxone (J01DD04)	–	–	–	–	18	3.9	–	–	–	–
Nitrofurantoin (J01XE01)	–	–	–	–	–	–	3	3.4	–	–
Benzathine benzylpenicillin (J01CE08)	–	–	–	–	–	–	3	3.4	–	–

When the durations of antibiotic therapy were analyzed by the most common four A. infections, it was found to be 6.54 ± 2.26 days (min: 1, max: 14 days) for A. pharyngitis; 6.50 ± 1.95 days (min: 2, max: 14 days) for A. bronchitis; 6.89 ± 2.37 days (min: 1, max: 14 days) for A. sinusitis and 7.26 ± 2.45 days (min: 1, max: 12 days) for A. tonsillitis. No statistically significant differences were found in the comparisons of the durations of antibiotic therapy for these indications ($p > 0.05$).

All prescriptions written out for A. infections were also examined in terms of generic-original antibiotic prescribing. A total of 359 antibiotics were prescribed for A. infections and 61.0% of them were generics. When the generic-original antibiotic prescribing was analyzed by health care facilities, except for PHs (48.8%), the percentage of generic antibiotic prescribing was higher in all and PHCFs had the highest (66.5%). In the comparisons of generic-original antibiotic prescribing by health care facilities, statistically significant differences were found ($p < 0.05$). These were due to a higher ratio of generic antibiotic prescribing in PHCFs and a higher ratio of original antibiotic prescribing in PHs than others. Generic antibiotics constituted 57.2% of the cost of all antibiotics that were prescribed for A. infections. A comparison of the costs of generic antibiotic prescribing and original antibiotic prescribing by health care facilities did not give out any statistically significant difference ($p > 0.05$), (Table 8).

For each of the most common four A. infections, generic-original antibiotic prescribing was examined. Accordingly, the percentage of generic antibiotic prescribing was found to be higher for all indications with the highest percentage for A. pharyngitis (65.7%) and the lowest percentage for A. sinusitis (51.7%). There were no statistically significant differences in the comparisons of generic-original for most common four A. infections ($p > 0.05$). The costs of generic and original

Table 6 Distribution of the ATC 4 classification of antibiotics by most frequently written for four acute (A.) infections.

ATC classification	A. pharyngitis		A. bronchitis		A. sinusitis		A. tonsillitis	
	n	%	*n*	%	*n*	%	*n*	%
Beta-lactam antibacterials, penicillins (J01C)	50	46.3	17	17.9	20	34.5	40	66.7
Other beta-lactam antibacterials (J01D)	37	34.3	32	33.7	21	36.2	16	26.7
Macrolides, lincosamides and streptogramins (J01F)	15	13.9	19	20.0	7	12.1	3	5.0
Quinolone antibacterials (J01M)	5	4.6	26	27.4	10	17.2	1	1.7
Other antibacterials (J01X)	–	–	1	1.1	–	–	–	–
Amphenicols (J01B)	1	0.9	–	–	–	–	–	–
Total	108	100.0	95	100.0	58	100.0	60	100.0

Table 7 Distribution of the most commonly prescribed ten antibiotics in each four acute (A.) infections.

Antibiotic (ATC 5 Code) (n = Total number of antibiotics)	A. pharyngitis (n = 108)		A. bronchitis (n = 95)		A. sinusitis (n = 58)		A. tonsillitis (n = 60)	
	n	%	*n*	%	*n*	%	*n*	%
Amoxicillin + clavulanic acid (J01CR02)	32	29.6	11	11.6	16	27.6	28	46.7
Cefuroxime (J01DC02)	10	9.3	15	15.8	4	6.9	6	10.0
Cefaclor (J01DC04)	7	6.5	–	–	4	6.9	2	3.3
Amoxicillin (J01CA04)	6	5.6	–	–	–	–	2	3.3
Azithromycin (J01FA10)	6	5.6	3	3.2	–	–	–	–
Sultamicillin (J01CR04)	5	4.6	4	4.2	2	3.4	–	–
Cefpodoxime (J01DD13)	5	4.6	4	4.2	3	5.2	–	–
Clarithromycin (J01FA09)	5	4.6	10	10.5	3	5.2	–	–
Cefditoren (J01DD16)	4	3.7	–	–	–	–	–	–
Cefalexin (J01DB01)	3	2.8	–	–	–	–	2	3.3
Gemifloxacin (J01MA15)	–	–	9	9.5	7	12.1	–	–
Moxifloxacin (J01MA14)	–	–	7	7.4	–	–	–	–
Levofloxacin (J01MA12)	–	–	7	7.4	–	–	–	–
Cefazolin (J01DB04)	–	–	5	5.3	–	–	–	–
Cefixime (J01DD08)	–	–	–	–	4	6.9	2	3.3
Cefprozil (J01DC10)	–	–	–	–	3	5.2	3	5.0
Miocamycin (J01FA11)	–	–	–	–	3	5.2	–	–
Combinations (J01CE30)	–	–	–	–	–	–	4	6.7
Benzathine benzylpenicillin (J01CE08)	–	–	–	–	–	–	3	5.0
Benzathine phenoxymethylpenicillin (J01CE10)	–	–	–	–	–	–	2	3.3

antibiotics prescribed for the most common four A. infections were examined. Accordingly, except for A. sinusitis (39.8%), in all infections, a large part of the total antibiotic cost belonged to generic antibiotics with the highest ratio for A. pharyngitis (64.3%). In the comparisons of the costs of generic antibiotic prescribing and original antibiotic prescribing by indications, statistically significant differences were found. Pertaining to the cost of the generic antibiotics, A. bronchitis was found to be different from others ($p < 0.05$). Pertaining to the cost of the original antibiotics, on the other side, a statistically significant difference was found between bronchitis and pharyngitis, tonsillitis; between pharyngitis and sinusitis; and between sinusitis and tonsillitis ($p < 0.05$), (Table 8).

4. Discussion

Evaluation of the prescriptions contributes to conduct effective strategies for the elimination of the IUA related problems. This is the first study which made an in-depth analysis of the antibiotic utilization by various health care facilities in 10 provinces of Turkey. Besides, the fact that the number of prescriptions per physician was found to be 2.3 serves as an important indicator of the performance of many physicians (535 physicians). This study also well reflects the antibiotic prescribing attitudes of almost all groups of physicians given the fact that one-third of the prescriptions was from primary health care while the second one-third from the internal medicine departments and the last one-third from the surgical medicine departments.

In this study, NDPP (3.2 drugs) was found to be close to the value (3.1 drugs) reported in the study which was carried out with the antibiotic prescriptions with a single diagnosis (Mollahaliloğlu et al., 2012).This may be related to the physicians' tendency to polypharmacy and also multi-diagnosed prescriptions written for some patients. For instance, a common trend to prescribe also analgesics, respiratory system medicines, etc. – in addition to antibiotics – for infections, can be the other underlying reason, as well. This is also

Table 8 Comparisons of generic and original antibiotics which were prescribed for acute infections by health care facilities and indications.

		Antibiotics			ACPP ($)			
		Generic %	Original %	Statistics	Statistics	Generic $ mean ± SD (%)	Original $ mean ± SD (%)	
Health care facilities (n = Total number of antibiotics)	PHCF (n = 191)	66.5 (n = 127)	33.5 (n = 64)	X^2 = 8.49 p = 0.037	Generic X^2 = 2.901 p = 0.407	16.3 ± 10.3 (62.0)	19.7 ± 16.8 (38.0)	PHCF (3318,10)
	PH (n = 86)	48.8 (n = 42)	51.2 (n = 44)			21.7 ± 23.6 (46.3)	22.9 ± 15.8 (53.7)	PH (1876,28)
	PTE-H (n = 63)	64.5 (n = 40)	35.5 (n = 23)		Original X^2 = 6.075 p = 0.108	15.0 ± 13.3 (61.1)	15.9 ± 11.7 (38.9)	PTE-H (881,50)
	UH (n = 19)	52.6 (n = 10)	47.4 (n = 9)			17.3 ± 19.2 (61.6)	12.0 ± 4.9 (38.4)	UH (280,44)
	Total (n = 359)	61.0 (n = 219)	39.0 (n = 140)			17.2 ± 14.3 (57.2)	19.6 ± 15.4 (42.8)	Total (6356,32)
Diagnoses (n = Total number of antibiotics)	Pharyngitis (n = 108)	65.7 (n = 71)	34.3 (n = 37)	X^2 = 3.19 p = 0.363	Generic X^2 = 24.28 p = 0.000	13.6 ± 8.8 (64.3)	14.2 ± 8.7 (35.7)	Pharyngitis (1474,8)
	Bronchitis (n = 95)	62.1 (n = 59)	37.9 (n = 36)			25.4 ± 19.8 (59.8)	27.0 ± 17.7 (40.2)	Bronchitis (2422,7)
	Sinusitis (n = 58)	51.7 (n = 30)	48.3 (n = 28)		Original X^2 = 21.830 p = 0.000	17.2 ± 12.0 (39.8)	27.0 ± 19.6 (60.2)	Sinusitis (1253,8)
	Tonsillitis (n = 60)	60.0 (n = 36)	40.0 (n = 24)			13.3 ± 10.5 (61.3)	11.9 ± 6.0 (38.7)	Tonsillitis (736,2)

Diagnoses (Total cost of antibiotics $)

Health care facilities (Total cost of antibiotics $)

supported by the fact that approximately half of the prescriptions (49.1%) included analgesics.

The prescriptions were mostly prescribed for respiratory tract infections (Table 1). Similarly, another study conducted in Turkey and two others conducted in Sweden and India also reported the same findings that antibiotics were mostly prescribed for respiratory tract infections (Aydın et al., 2005; Lundborg et al., 2002; Pathak et al., 2011).

NDPP is one of the drug utilization indicators (WHO, 2002). NDPP was found to be 3.23 and it was highest in PHCFs (3.34), ($p < 0.05$), (Table 2). This may be related to the tendency toward prescribing other medicines in PHCFs instead of prescribing a number of antibiotics. When the details of antibiotic prescribing patterns are evaluated, this finding also becomes more clear. One-third of all medicines were antibiotics (34.8%). NAPP was 1.12 for all health care facilities, being highest (1.21) in PTE-Hs ($p < 0.05$); and lowest (1.04) in PHCFs (Table 2). In a study which was conducted in a training hospital in Turkey, NAPP was 1.05 and 3.7% of the antibiotics were the injectable (Avci et al., 2006). This value, which was reported in a training hospital, is lower than that found in UHs (1.19) in this study. On the other hand, considering 7.3% of the antibiotics were the injectable forms, it can be deduced that the number of parenteral antibiotics was also higher. The findings, which figured out the fact that 10.6% of all prescriptions gave out injectable antibiotics and the injectable antibiotics constituted three-fourth of these medicines, also support the view that physicians, in general, are inclined to prescribe parenteral antibiotics.

The cost of the prescribed medicines is also an important drug utilization indicator which is significant and therefore used in making an assessment of the RUD performance of the physicians (Holloway and van Dijk, 2011; WHO, 2002; De Vries et al., 1994). The study indicated that CPP was 33.32 $ with the highest-cost prescriptions written out in PHs ($p < 0.05$) and the lowest-cost prescriptions written out in PHCFs (Table 2). As for the cost of the prescribed antibiotics, it constituted half of the cost of all prescriptions (50.2%). ACPP was 16.73 $, with the highest-cost prescriptions written out in PHs and PTE-Hs (17.87 $ and 17.71 $, respectively), ($p < 0.05$) and with the lowest-cost antibiotics written out in PHCFs. While NDPP was found highest in PHCFs; NAPP, CPP and ACPP were lowest in PHCFs (Table 2). Perhaps, it is because PHCFs rather prefer generics that are less expensive (Table 8). In addition, as stated above, PHCFs are also inclined to prescribe other drugs (usually the drugs that are less costly than antibiotics). Physicians practicing in PHCFs, for instance, are more in favor of prescribing additional drugs such as respiratory system medicines, analgesics, etc. Another study that reported the use of medicines for respiratory tract infections in children in Turkey, similarly pointed out that the respiratory system medicines were the second most commonly prescribed medicines following antibiotics (Akici et al., 2004). Apart from these, PHCFs also provide patients with treatment of other diseases, which can be associated with the lower antibiotic prescribing rates in PHCFs. In fact, it was found out that the prescribing rates for gastrointestinal system and cardiovascular system medicines which were often subject of the prescription repeat, were higher in PHCFs than hospitals (Table 3).

The most common diagnosis on the prescriptions was the respiratory system infections and most of them were the upper

respiratory tract infections. While assessing the prescriptions, it was assumed that the diagnoses were correct. On the other hand, the unavailability to take an additional initiative aiming to verify the accuracy of the diagnosis and to check if the antibiogram tests were given to patients before prescribing antibiotics can be considered as limitations of this study. The study was conducted in November–December, when infectious diseases were common, and did not comprise the remaining ten months of a year's time can be considered another limitation.

Penicillins, ''other beta-lactams'' and quinolones were the most commonly prescribed antibiotics on prescriptions. In PHCFs and UHs, penicillins were the most commonly prescribed antibiotics while it was ''other beta-lactams'' in PHs and PTE-Hs (Table 4). According to the Intercontinental Medical Statistics (IMS) Health Turkey data, penicillins were the most commonly prescribed antibiotics in 2001–2006. In this period, the use of antibiotics had a steady increase particularly in cephalosporins, quinolones, macrolides and lincosamides (Karabay and Hosoglu, 2008). Given the higher prescribing rates of these groups of antibiotics as pointed out by this study, the afore-mentioned trend of increase is still continuing. In the literature, there is a wide range of groups of antibiotics that are commonly used; some groups of antibiotics, particularly penicillins are much more prescribed. A study which analyzed different literatures published between 2000 and 2005 years, reported that penicillins and macrolides were commonly used antibiotics for pediatric patients (Rossignoli et al., 2007). A study, which was carried out with GPs in Denmark and Spain, figured out that most GPs in Denmark prescribed narrow-spectrum penicillins, followed by macrolides and wide-spectrum antibiotics while most GPs in Spain prescribed wide-spectrum penicillins, amoxicillin and beta-lactamase inhibitor combinations for respiratory tract infections. However, the ''quinolone antibacterials'', which occupied the third rank in our study, were not commonly prescribed in Denmark and Spain (Bjerrum et al., 2004). A point prevalence study, which was carried out on inpatients in pediatric hospitals in Turkey, revealed that cephalosporins and penicillins were the most commonly used antibiotics while another study carried out in PHCFs pointed out to beta-lactamase inhibitor combinations and macrolides being the most commonly used antibiotics (Ceyhan et al., 2010; Akici et al., 2004). Another study, which was carried out in the secondary health care level in Kyrgyzstan, reported that beta-lactam antibacterials-penicillins, aminoglycosides and cephalosporins were the most commonly prescribed antibiotics (Baktygul et al., 2011).

In Mexico, a study analyzing the use of antibiotics for the upper respiratory tract infections in under 16-aged patients in private health care indicated that penicillins, cephalosporins and macrolides were the most commonly used antibiotics (Peláez-Ballestas et al., 2003). A study conducted in a training hospital in Turkey found out that co-amoxiclav, quinolones and cephalosporins were the most commonly prescribed antibiotics (Avci et al., 2006). In India, a study analyzing the pediatric patients in the tertiary care level reported cephalosporins as the most commonly prescribed antibiotics (Sharma et al., 2009). Another study conducted in the tertiary care level in Nepal reported macrolides, fluoroquinolones and beta-lactams as the most commonly prescribed antibiotics (Kumar et al., 2010). As a result, like a number of other national and international studies in the literature this study also points out that the physicians rather prefer wide-spectrum antibiotics.

Amoxicillin + clavulanic acid and cefuroxime were reported to be the most commonly prescribed antibiotics in all health care facilities (Table 5). This is another finding that implies that physicians rather prefer wide-spectrum antibiotics. A study, which was conducted in PHCFs in Croatia, reported amoxicillin, co-amoxiclav and co-trimoxazole as the most commonly prescribed antibiotics (Vojvodić, 2010). A study, which was conducted in PHCFs in Denmark and Italy, reported that in Denmark, phenoxymethylpenicillin and amoxicillin; in Italy, amoxicillin and amoxicillin + enzyme inhibitor combination were the most commonly prescribed antibiotics (Vaccheri et al., 2002). A study with family physicians from Poland reported that amoxicillin, amoxicillin + clavulanic acid and cefuroxime were the most commonly prescribed antibiotics for respiratory tract infections (Chlabicz et al., 2004). A study conducted in PHCFs in Western China indicated that amoxicillin, benzylpenicillin and norfloxacin were the most commonly prescribed antibiotics (Dong et al., 2008). A comprehensive survey on the use of antibiotics in 15 European countries between 1997 and 2002 concluded that the share of co-amoxiclav use in the total use of penicillins increased over years (Vander Stichele et al., 2006). The study from Kyrgyzstan, reported that penicillin G, gentamicin and metronidazole were the most commonly used antibiotics (Baktygul et al., 2011). The study from Mexico, indicated that amoxicillin + clavulanic acid was the most commonly used antibiotic (Peláez-Ballestas et al., 2003). Another study conducted in the tertiary care level in Nepal reported azithromycin, ciprofloxacin and amoxicillin as the most commonly prescribed antibiotics (Kumar et al., 2010). A study, which was conducted in the tertiary care level in Turkey, pointed out to ciprofloxacin being the most commonly used antibiotic (Yapar et al., 2006). Accordingly, developed by the findings of all these studies available in the literature, it is interesting that amoxicillin, which is among the most commonly used antibiotic in general, had a lower prescribing rate in our study and was not even prescribed in health care facilities except for PHCFs (Table 5).

The most common four A. infections were also analyzed in terms of antibiotic utilization patterns. Accordingly, mostly prescribed antibiotics were found as penicillins for A. pharyngitis and A. tonsillitis and ''other beta-lactams'' for A. bronchitis and A. sinusitis (Table 6). It could be asserted that the studies in the literature have great variations in antibiotics that are preferred specifically for different indications and, in partial, are similar to our findings. For instance, a study conducted in PHCFs in Turkey reported that beta-lactam and beta lactamase inhibitors and oral cephalosporins were the most commonly prescribed antibiotics for A. pharyngitis and A. sinusitis (Leblebicioglu et al., 2002). Another study conducted in PHCFs in Italy reported that macrolides, cephalosporins, penicillins + beta lactamase inhibitor combinations and wide-spectrum penicillins were the most commonly prescribed antibiotics for acute respiratory tract infections (Mazzaglia et al., 1998). A study with GPs in Denmark and Spain, figured out that most GPs in Denmark prescribed penicillin V for most A. tonsillitis cases while most GPs in Spain prescribed wide-spectrum penicillins and macrolides (Bjerrum et al., 2004).

Although the placement of the most common antibiotic groups prescribed for A. sinusitis was different from those prescribed for A. pharyngitis and A. tonsillitis; amoxicillin + clavulanic acid was found to be the most commonly

prescribed group for all three infections. Cefuroxime was found to be the most commonly prescribed antibiotic for A. bronchitis (Table 7). A study conducted in the PHCFs in Croatia indicated amoxicillin as the most commonly prescribed antibiotic for A. pharyngitis and A. tonsillitis while another study conducted in Italy indicated azithromycin as the most commonly prescribed antibiotic for both indications (Vojvodić, 2010; Mazzaglia et al., 1998). The study from Croatia revealed that co-amoxiclav was the most commonly prescribed antibiotic for A. bronchitis and A. sinusitis while a Polish study revealed that cefuroxime was the most commonly prescribed antibiotic for A. bronchitis and it was amoxicillin + clavulanic acid for A. sinusitis (Vojvodić, 2010; Chlabicz et al., 2004). Another study, which was conducted with pediatric patients diagnosed with acute respiratory tract infection at hospitals in Spain, reported amoxicillin + clavulanic acid, amoxicillin and cefuroxime as the most commonly prescribed antibiotics (Ochoa et al., 2001). In this study, on the other hand, amoxicillin occupied the fourth rank for A. pharyngitis and the sixth rank for A. tonsillitis whereas it was not included in the first 10 antibiotics prescribed for A. sinusitis. A recent randomized controlled trial, which compared amoxicillin with placebo in the treatment of A. rhinosinusitis indicated that amoxicillin provided little clinical benefit (Garbutt et al., 2012). Cochrane review commented that various groups of antibiotics created similar effects in the treatment of A. sinusitis and neither of them had advantages over the others. In new generation and wide-spectrum antibiotics, the long term effectiveness is reported to be similar, however, further adverse effects are reported for the use of amoxicillin + clavulanic acid than cephalosporins and macrolides (Ahovuo-Saloranta et al., 2011). A meta-analysis reported that in the treatment of A. sinusitis the more recent fluoroquinolones did not turn out to be more advantageous than beta-lactam antibiotics (Karageorgopoulos et al., 2008). The NICE Guideline of the United Kingdom does not recommend prescribing antibiotics for A. bronchitis except for some specific conditions (NICE, 2008). Cochrane review acknowledged that satisfactory evidence, which clearly supports the effectiveness of using antibiotics for A. bronchitis, is limited (Smith et al., 2011). Cochrane review recommends using penicillins primarily for the treatment of A. streptococcal pharyngitis in children and adults (van Driel et al., 2011). In children who have penicillin allergy, cephalosporins are suggested for use as an alternative to penicillins (Regoli et al., 2011). In the light of these findings, it is apparent that physicians, like in most other cases, were more likely to prescribe wide-spectrum antibiotics for the four acute infections reviewed in this study. This likelihood seems even much more apparent in this study than other studies in the literature. When the recent debates on whether antibiotics are required for treatment of these infections or any differences exist between the patterns of treatment with different groups of antibiotics are also taken into consideration, the findings in this study reveal the importance of the physicians' attention while prescribing antibiotics. The fact that the highest costs of treatment were caused by the prescription of antibiotics puts further emphasis on the importance of rational antibiotic prescribing, as well.

Patients can have non-compliance with antibiotic treatment for several reasons. Long-term antibiotic treatment is among these reasons. For instance, a study conducted in Mexico reported that patients' non-compliance with antibiotic treatment was relevant to the treatment schemes that took more than 7 days (Kardas, 2002, 2006; Kardas et al., 2005; Reyes et al., 1997). In this study, the average duration of antibiotic therapy was found to be about 7 days for A. infections. A French study, which made an assessment of antibiotic prescribing, reported an average of 8 days for an antibiotic treatment scheme (Guillemot et al., 1998). It was found out that average duration of antibiotic therapy was more than 7 days for A. tonsillitis, and it took approximately 7 days for A. pharyngitis, A. bronchitis and A. sinusitis. A survey conducted in PHCFs in Poland found out that physicians usually prescribed antibiotic treatment for 7.2 days for A. tonsillitis and for 8 days for sinusitis (Windak et al., 1996). A randomized controlled study, which was conducted on the patients diagnosed with A. rhinosinusitis and treated with amoxicillin, reported lower clinical benefits for 10-day amoxicillin treatment schedules in most of the patients (Garbutt et al., 2012).

Most of the antibiotics prescribed for A. infections were generics (61.0%) and the generic antibiotic prescribing rates were higher than original antibiotic prescribing in all health care facilities except for PHs ($p < 0.05$), (Table 8). On the other hand, CPP was found to be highest in PHs ($p < 0.05$), (Table 2). Perhaps, it is because PHs had higher original antibiotic prescribing rates. The cost of generic antibiotics constituted 57.2% of total cost of the antibiotics that were prescribed for A. infections (Table 8). For all of four A. infections, the generic antibiotic prescribing rates were higher than the original antibiotic prescribing rates (Table 8). The use of generic drugs is becoming more popular in the world and it is commonly used as an option to reduce the higher costs of treatments with originals (Weekes and Ramzan, 2010; García Rada, 2011; Godman et al., 2010; Tsiantou et al., 2009; Decollogny et al., 2011). This study also indicates that the physicians in Turkey, in general, are more inclined to prescribe generic antibiotics than originals.

5. Conclusions

This study made a detailed assessment of the prescriptions containing antibiotics prescribed in various health care facilities in different provinces across Turkey and gave out some interesting findings about the antibiotic utilization. Although a higher number of medicines were prescribed in PHCFs than other health care facilities, either CPP or ACPP was found to be lowest. Physicians' tendency of prescribing generic medicines in PHCFs can also serve as an underlying reason for this, in partial. Physicians usually prescribed antibiotics for about one week's time and all health care facilities rather preferred wide-spectrum antibiotics and beta-lactamase combinations, in particular. It is considered that this study, in the context of health care facilities and indications, will guide decision-makers to scale-up the rational use of antibiotics and reimbursement systems to provide sustainable services in the country.

Authors' contributions

This study was carried out collaboratively by all authors. Mollahaliloglu conducted and managed the research report which is the basis of this article with Akici, Alkan and Ozgulcu. Akici and Alkan analyzed the data. Donertas contributed to the data

analysis and preparation of the article. Akici and Mollahaliloglu structured the article. Donertas and Ozgulcu helped to interpret the study results and review the drafts and the final version of the article. Mollahaliloglu and Akici led the preparation of the final manuscript. All authors read and approved the article.

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