

FACTORS AFFECTING THE MEDICATION ADHERENCE OF THE PATIENTS WHO ARE PRESCRIBED ANTIBIOTICS

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ABSTRACT

Aim: In this study, our aim is to investigate the antibiotics adherence of the patients who are prescribed antibiotics.

Methods: This study was conducted on 353 patients between age 18-75 who were prescribed antibiotic and who were registered to Bursa Nilufer 23 Nisan Family Health Center between dates October 2018-September 2019, following the ethics committee approval. In order to collect data in this study, beside the medical history, Socio-demographic Data Form, Morisky Medication Adherence Scale and short version of European Health Literacy Scale which questioned their antibiotics adherence were applied to the patients.

Results: Medication utilization loyalty was detected significantly higher in the participants with high health literacy. The disease for which antibiotics were most frequently prescribed was upper respiratory infection (32.3%). It was followed by lower respiratory infections (23.5%), acute sinusitis (13%) and urinary tract infections (7.6%) respectively. Most commonly prescribed antibiotics were cephalosporines (32.3%), penicillin (29.5%) and macrolides (23.2%). The most common side effect was diarrhea (30.4%). Whereas high adherence rate was significantly high in the patients without fever, medium adherence rate was detected significantly higher in patients with fever. Percentage of high adherence was significantly high in case the antibiotic was recommended by the family physician.

Conclusions: Antibiotic adherence is quite high in our region. Health literacy levels of the patients are associated with their medication adherence. Antibiotics recommended by the family physicians were used more regularly. Family physicians must behave more carefully about rational drug use, must have a full knowledge of the guides and must meet the requirements of modern medicine.

Keywords: Rational drug use, rational antibiotic use, health literacy, medication adherence, family medicine

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Received: December 22, 2021; **Accepted:** December 29, 2021; **Published Online:** December 31, 2021

Cite this article as: Akkaya, U. & Demirci, H. (2021). Factors Affecting The Medication Adherence of the Patients Who Are Prescribed Antibiotics 1(3), 93-107.



Introduction

According to the estimation of World Health Organization (WHO), more than half of all medications are prescribed, distributed and sold inconveniently. Nearly half of the patients do not use medications properly and one third of the world population can't reach basic medications (1). Wrong drug use is common in developed countries and in our country both medically and economically. Antibiotics are at the top of these misused drugs.

According to the 2013 data of our Ministry of Health, it is reported that nearly 25.9% of all health expenses in Turkey were allocated to medication charges and this rate is around 10-15% in European countries and around 20-40% in developing countries (2). A high share is allocated to medication expenses in our country, among the reasons of this situation we can list the following causes; therapeutic medicine applications in the forefront, undeveloped preventive medicine applications, inattention of rational drug use, external dependence in pharmaceutical industry, inadequacy of health literacy (HL) rate, excess use of antibiotics.

Antibiotics are used in treatment of human and animal health, animal feeds and plants worldwide. Antibiotics are among the most frequently used medications in the world and in our country. Despite the introduction of medication tracking system and prohibition of non-prescription antibiotic sales in our country in recent years, antibiotics are still in the first rank among the drugs sold (3). Antibiotics consumed unconsciously are the most important elements of drug wastage in our country. When this wastage is considered together with developing antibiotic resistance and its economic cost effect, importance of Rational Antibiotic Use (RAU) increases.

Health literacy level is critical in RAU. As antibiotics are technological products of great importance in preventing individual and social infection diseases and fighting against these diseases, rational use of this valuable source is essential in terms of public health (5). There are several reasons in irrational antibiotic use such as lack of socio-cultural, economic and regulatory health policies together with lack of education as well as insufficiency of inter-sector cooperation. These reasons affect each other and the problems become more complicated (6). Patients request antibiotics redundantly from the physicians and physicians can prescribe antibiotics due to time constraints and pressure. Misdiagnosis, antibiotics used in low dose, short time and period increase the antibiotic resistance in bacteria. In this study, our aim is to investigate the factors affecting antibiotic adherence of the patients who are prescribed antibiotics. In the literature, importance of RAU is increasing day by day with bacteria resistance problem and with its economic and social aspect.

In this study, our aim is to investigate the factors affecting antibiotic adherence of the patients who are prescribed antibiotics.

METHODS

The dissertation named "Factors affecting the medication adherence of the patients who are prescribed antibiotics" was approved by the Clinical Research Ethics Committee of Bursa Yuksek Ihtisas Training and Research Hospital, University of Health Sciences, with the resolution and approval dated 29.08.2018, no2011-KAEK-25 2018/08-09.

This research was planned as a monocenter, descriptive, observational study. This study was performed between 01.10.2018-30.09.2019. Before being included in the study, each participant was informed about the aim of the study and they were

asked to sign the volunteer consent form. In our study, a questionnaire was applied to 353 participants through face-to-face interviews. Socio-demographic data form configured by us, Morisky Medication Adherence Scale and short form of European Health Literacy Scale were used to collect data in the study. Face-to-face interviews were conducted with the participants of the study and questions in the questionnaires were addressed to them, later, on the day of the end of antibiotic use, the remaining questions about drug adherence were asked to the participants face-to-face or via telephone.

Patients between age 18-75, registered to Bursa Nilufer 23 Nisan Family Health Center and who were prescribed antibiotics by 4 Family Physicians working in this institution and single-diagnosed patients between age 18-75, registered to Family Health Center but who were recommended to use antibiotics by the physicians in health institutions other than those in FHC (specialist physicians, dentist, emergency physicians working in hospital etc.) were included in this study.

The first part of the questionnaire consists of questions about socio-demographic information (age, gender, profession, marital status, education level, income level) and medical status of the patient (chronic diseases, complaints, time of complaints, whether or not he/she took medications for the complaints, diagnosis, who recommended the antibiotic, name of the antibiotic, dosage, recommended time of use, use of administration, number of days to use the antibiotic, side effects, type of side effects, number of medications used for chronic disease if exists, number of labor lost days, whether or not he/she used the antibiotic for a short time, if yes number of lacking days and reason) and it is attached.

Morisky Medication Adherence Scale: this scale was developed by Morisky, Gren and Levine (1986) with

the aim of evaluating the medication adherence of the individuals with chronic disease in a short and accurate way (7). Following questions which were adapted to antibiotic use were posed to the participants about their antibiotic use adherence and their Morisky adherence statuses were grouped in accordance with their scores. This is a self-report consisting of four questions. Turkish validity and reliability study of the scale was performed by Bahar et al.(8).

Short Version of European Health Literacy Scale: Short version of European health literacy was used in our study (9). 16 questions with five choices as "very difficult, fairly difficult, fairly easy, very easy, I don't know" were asked to the participants to measure their HL levels. These choices were scored as; very difficult 1 point, fairly difficult 2 points, fairly easy 3 points, very easy 4 points and I don't know 0 point. The results were grouped in 4 levels according to the total scores as; inadequate HL, problematic HL, sufficient HL and excellent HL. Turkish validity and reliability study of the scale was performed by Emiral et al. (10).

Statistical Analysis of the Data: Data achieved were analyzed with SPSS Statistical Package® 22.0 program. In all statistical analysis $p < 0.05$ was accepted as significance level and the relationships were evaluated within 95% confidence interval. Descriptive data of the study group were expressed with number and percentage for distribution of categorical variables and with mean, standard deviation, median, minimum and maximum for continuous variables. Conformity to normal distribution was checked with Kolmogorov Smirnov and Shapiro Wilk tests. Relationship between categorical dependent and independent variables was assessed with chi-square test and Fisher-Freeman-Halton tests and relationship between numerical and categorical variables were assessed with Kruskal Wallis tests. Bonferroni correction was applied in post-hoc analysis.

RESULTS

General characteristics of the participants are given in Table1. Mean age was 40.83 and 68.0% of

the participants were female. 55.2% of the cases were bachelor’s degree.

Table1. Distribution according to socio-demographic features

		Number of participants		%	
Gender	Female	240		68.0	
	Male	113		32.0	
Income	Low	5		1.4	
	Medium	233		66.0	
	High	115		32.6	
Marital Status	Single	62		17.6	
	Married	291		82.4	
Profession	Unemployed	4		1.1	
	Housewife	89		25.2	
	Staff	80		22.7	
	Retired	38		10.8	
	Student	20		5.7	
	Worker	93		26.3	
	Craftsman	29		8.2	
Education	Illiterate	2		0.6	
	Primary school	34		9.6	
	Secondary school	26		7.4	
	High school	96		27.2	
	University	195		55.2	
Age	Mean	Standard Deviation	Median	Minimum	Maximum
	40.83	12.79	39.00	18.00	75.00

Medication adherence was detected significantly higher in the participants with high HL level (Table2).

Table2. Morisky Medication Adherence and European Health Literacy Scale correlations

Correlation coefficient	-0.156
p value	0.003*

*Spearman correlation analysis

The disease for which antibiotics were most frequently prescribed was upper respiratory infection (32.3%). It

was followed by lower respiratory infections (23.5%), acute sinusitis (13.0%) and urinary tract infections (7.6%) respectively (Figure1).

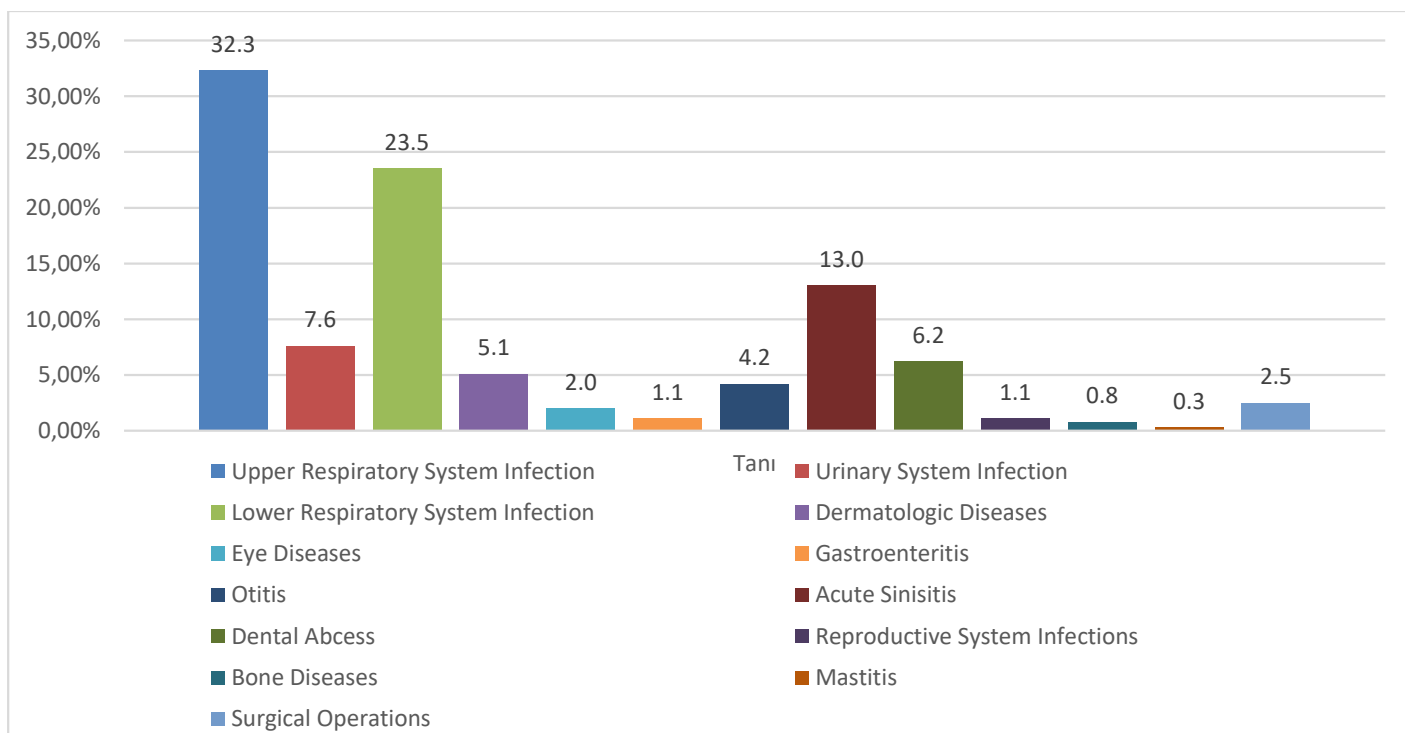


Figure1. Case distribution according to diagnosis

Most commonly prescribed antibiotics were Cephalosporines (32.3%), Penicillin (29.5%) and Macrolides (23.2%) (Figure2).

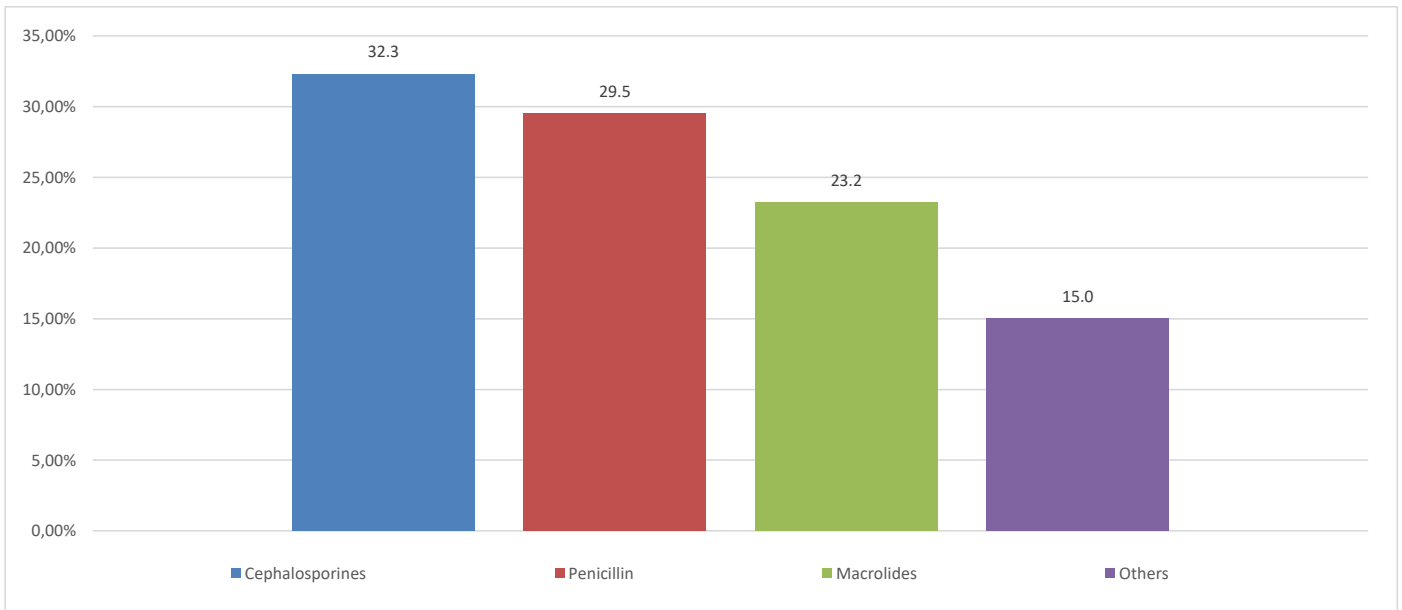


Figure2. Distribution of the antibiotics used

Most prevalent side effect was gastrointestinal complaints (Figure 3). It was followed by itchy skin and allergic reactions.

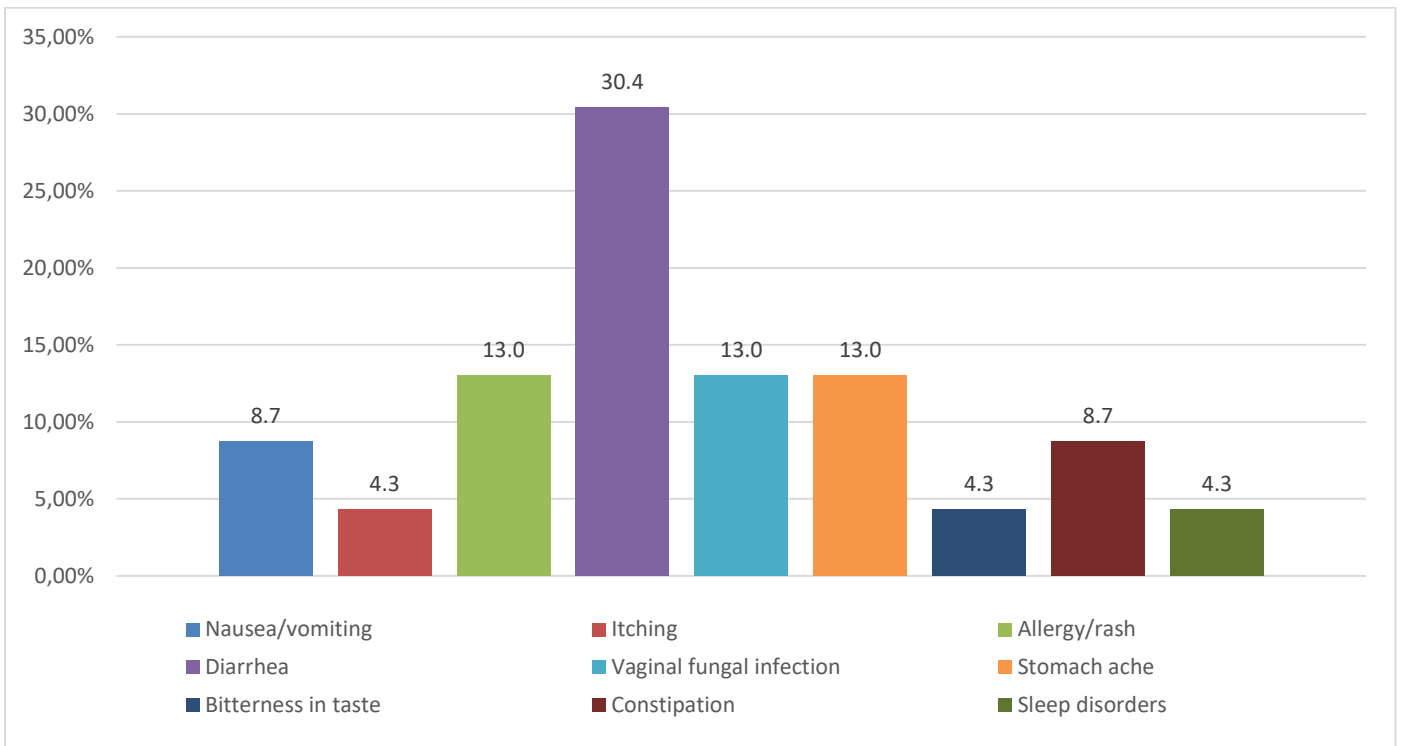


Figure3. Distribution according to side effects

Whereas high adherence rate was significantly high in the patients without fever, medium adherence rate was detected significantly higher in patients with fever (Table 3). Percentage of high adherence was

significantly high in case the antibiotics were recommended by the family physician (Table 3 and Figure 4)

Table3. Disease and antibiotic categories and adherence scale categories

		Medication Adherence						p-value
		High		Medium		Low		
		n	%	n	%	n	%	
Chronic disease	No	188	73.2	58	22.6	11	4.3	0.731*
	Yes	74	77.1	19	19.8	3	3.1	
Headache	No	138	74.6	42	22.7	5	2.7	0.425*
	Yes	124	73.8	35	20.8	9	5.4	
Nasal flow	No	170	77.6	41	18.7	8	3.7	0.168*
	Yes	92	68.7	36	26.9	6	4.5	
Nasal obstruction	No	156	77.2	40	19.8	6	3.0	0.268*
	Yes	106	70.2	37	24.5	8	5.3	
Sneezing	No	169	75.8	46	20.6	8	3.6	0.668*
	Yes	93	71.5	31	23.8	6	4.6	
Swollen tonsils	No	185	73.4	56	22.2	11	4.4	0.779*
	Yes	77	76.2	21	20.8	3	3.0	
Cryptic Tonsillitis	No	252	74.6	73	21.6	13	3.8	0.409^
	Yes	10	66.7	4	26.7	1	6.7	
Cough	No	124	75.2	35	21.2	6	3.6	0.917*
	Yes	138	73.4	42	22.3	8	4.3	
Lymphadenopathy	No	259	74.2	76	21.8	14	4.0	-
	Yes	3	75.0	1	25.0	0	0.0	
Drug usage	No	155	73.8	50	23.8	5	2.4	0.120*
	Yes	107	74.8	27	18.9	9	6.3	
Fever	No	177	78.3	40	17.7	9	4.0	0.043*

	Yes	85	66.9	37	29.1	5	3.9	
Antibiotics	Cephalosporines	79	69.3	29	25.4	6	5.3	0.800 [^]
	Penicillin	82	78.8	19	18.3	3	2.9	
	Quinolone	21	72.4	8	27.6	0	0.0	
	Macrolides	62	75.6	16	19.5	4	4.9	
	Other	18	75.0	5	20.8	1	4.2	
Penicillin	No	180	72.3	58	23.3	11	4.4	0.426*
	Yes	82	78.8	19	18.3	3	2.9	
Who prescribed the antibiotic?	Family physician	199	77.1	53	20.5	6	2.3	0.016*
	Other physicians	63	66.3	24	25.3	8	8.4	
Dosage	1.00	57	73.1	16	20.5	5	6.4	0.743 [^]
	2.00	183	74.1	55	22.3	9	3.6	
	3.00	22	78.6	6	21.4	0	0.0	
Routes of administration	Oral	215	75.4	60	21.1	10	3.5	0.352 [^]
	Intramuscular	35	67.3	14	26.9	3	5.8	
	Dermal	5	71.4	2	28.6	0	0.0	
	Ophthalmic	6	85.7	0	0.0	1	14.3	
	External ear	1	50.0	1	50.0	0	0.0	
Routes of administration	Oral	215	75.4	60	21.1	10	3.5	0.435*
	IM	35	67.3	14	26.9	3	5.8	
Side effects	No	246	74.5	70	21.2	14	4.2	0.389*
	Yes	16	69.6	7	30.4	0	0.0	
Loss of labor	No	217	74.6	63	21.6	11	3.8	0.908*
	Yes	45	72.6	14	22.6	3	4.8	
Using in short time and dose	No	254	96.9	65	84.4	10	71.4	<0.001*
	Yes	8	3.1	12	15.6	4	28.6	

*Chi-square test, ^Fisher Freeman Halton; n: number of participants.

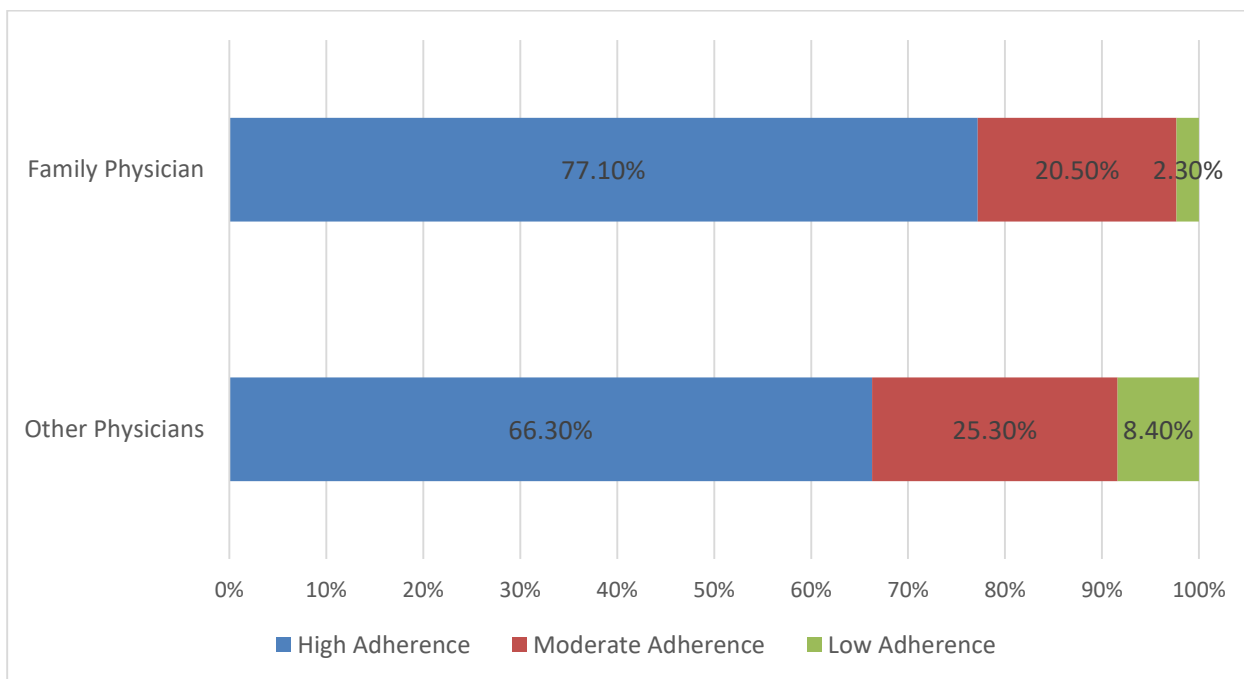


Figure4. Morisky scale categories according to the physician who recommends the antibiotic

Health literacy was similar in terms of gender, income, marital status and profession groups. Excellent HL rate

of the primary school graduates was significantly lower than high school and university graduates.

Table4. European Health Literacy Scale Categories according to socio-demographic feature

		Health Literacy						p-value
		Problematic		Sufficient		Excellent		
		Number	%	Number	%	Number	%	
Gender	Female	1	0.4	81	33.8	158	65.8	0.164 [^]
	Male	3	2.7	35	31.0	75	66.4	
Income	Low	0	0.0	4	80.0	1	20.0	0.175 [^]
	Medium	3	1.3	78	33.5	152	65.2	
	High	1	0.9	34	29.6	80	69.6	
Marital status	Single	1	1.6	20	32.3	41	66.1	0.794 [^]
	Married	3	1.0	96	33.0	192	66.0	

Profession	Unemployed	0	0.0	2	50.0	2	50.0	<0.001[^]
	Housewife	0	0.0	39	43.8	50	56.2	
	Staff	0	0.0	19	23.8	61	76.3	
	Retired	1	2.6	11	28.9	26	68.4	
	Student	1	5.0	7	35.0	12	60.0	
	Worker	1	1.1	27	29.0	65	69.9	
	Craftsman	1	3.4	11	37.9	17	58.6	
Education	Illiterate	0	0.0	2	100.0	0	0.0	<0.001[^]
	Primary School	0	0.0	25	73.5	9	26.5	
	Secondary School	1	3.8	10	38.5	15	57.7	
	High School	3	3.1	34	35.4	59	61.5	
	University	0	0.0	45	23.1	150	76.9	

Rate of swollen tonsils was higher in the group with excellent HL among the participants (Table5). HL level was higher in those with daily dose of 3.

Correlation of Morisky Scale and European Health Literacy Scale numerical values was calculated as 83.8%.

Table5. European Health Literacy Scale and disease and patient characteristics

		Health Literacy						p-value
		Problematic		Sufficient		Excellent		
		Number	Percentage	Number	Percentage	Number	Percentage	
Chronic disease	No	4	1.6	82	31.9	171	66.5	0.599 [^]
	Yes	0	0.0	34	35.4	62	64.6	
Headache	No	0	0.0	60	32.4	125	67.6	0.122 [^]
	Yes	4	2.4	56	33.3	108	64.3	
Nasal flow	No	1	0.5	78	35.6	140	63.9	0.114 [^]
	Yes	3	2.2	38	28.4	93	69.4	

Nasal obstruction	No	1	0.5	68	33.7	133	65.8	0.457 [^]
	Yes	3	2.0	48	31.8	100	66.2	
Sneezing	No	1	0.4	78	35.0	144	64.6	0.160 [^]
	Yes	3	2.3	38	29.2	89	68.5	
Swollen tonsil	No	3	1.2	94	37.3	155	61.5	0.015[^]
	Yes	1	1.0	22	21.8	78	77.2	
Cryptic Tonsillitis	No	4	1.2	113	33.4	221	65.4	0.498 [^]
	Yes	0	0.0	3	20.0	12	80.0	
Cough	No	1	0.6	59	35.8	105	63.6	0.415 [^]
	Yes	3	1.6	57	30.3	128	68.1	
Lymphadenopathy	No	4	1.1	115	33.0	230	65.9	-
	Yes	0	0.0	1	25.0	3	75.0	
Drug usage	No	1	0.5	71	33.8	138	65.7	0.406 [^]
	Yes	3	2.1	45	31.5	95	66.4	
Fever	No	3	1.3	74	32.7	149	65.9	-
	Yes	1	0.8	42	33.1	84	66.1	
Antibiotic	Cephalosporines	0	0.0	37	32.5	77	67.5	0.551 [^]
	Penicillin	2	1.9	31	29.8	71	68.3	
	Quinolone	0	0.0	13	44.8	16	55.2	
	Macrolides	2	2.4	25	30.5	55	67.1	
	Other	0	0.0	10	41.7	14	58.3	
Physician who recommends antibiotic	Family physician	4	1.6	86	33.3	168	65.1	0.623 [^]
	Other physicians	0	0.0	30	31.6	65	68.4	
Dosage	1	1	1.3	18	23.1	59	75.6	0.020[^]
	2	2	0.8	93	37.7	152	61.5	
	3	1	3.6	5	17.9	22	78.6	

Use of administration	Oral	4	1.4	96	33.7	185	64.9	0.070 [^]
	Intramuscular	0	0.0	13	25.0	39	75.0	
	Dermal	0	0.0	6	85.7	1	14.3	
	Ophthalmic	0	0.0	1	14.3	6	85.7	
	External ear	0	0.0	0	0.0	2	100.0	
Use of administration	Oral	4	1.4	96	33.7	185	64.9	0.371 [^]
	Intramuscular	0	0.0	13	25.0	39	75.0	
Side effect	No	4	1.2	107	32.4	219	66.4	0.731 [^]
	Yes	0	0.0	9	39.1	14	60.9	
Loss of labor	No	4	1.4	94	32.3	193	66.3	0.893 [^]
	Yes	0	0.0	22	35.5	40	64.5	
Using in short time and dose	No	4	1.2	106	32.2	219	66.6	0.529 [^]
	Yes	0	0.0	10	41.7	14	58.3	

DISCUSSION

As a result of this study, medication adherence was detected significantly higher in the participants with high HL. The disease for which antibiotics were most frequently prescribed was upper respiratory infection (32.3%). It was followed by lower respiratory infections (23.5%), acute sinusitis (13.0%) and urinary tract infections (7.6%) respectively. Most commonly prescribed antibiotics were Cephalosporines (32.3%), Penicillin (29.5%) and Macrolides (23.2%). The most common side effect was diarrhea (30.4%). Rate of high adherence was significantly high in the patients without fever. Medication dose and swollen tonsil was associated with HL. High adherence rate was significantly high in case the antibiotic was prescribed by the family physician.

According to our study, most commonly prescribed antibiotics were Cephalosporines (32.3%), Penicillin

(29.5%), Macrolides (23.2%) and Quinolones (8.2%) and this result was inconsistent with the literature. In the study called "Rational prescription of antimicrobials among family physicians and specialists: attitudes and demands" conducted by Çöplü et al. they were ranked as Penicillin (67.8%), Cephalosporines (36.3%), Macrolides (13.8%), Quinolones (9.59%) (11). In this current study, it was detected that physicians didn't use "Ministry of Health Diagnostic and Therapeutic Guide for Primary Care" at a high rate of 56% while prescribing antibiotics. In another study conducted in a health center in Mersin, it was reported that the most common diagnosis on patients was acute respiratory system infection (32.4%) and Penicillin (56.1%), Macrolides (21.9%) and Cephalosporines (11.5%) were the antibiotics prescribed (12). On the other hand, in the study performed by Döşler et al. in 2014 in Istanbul called "RAU: A sample from İstanbul", physicians participating in the study indicated that they

preferred Penicillin around 60% and Cephalosporines around 35% (13). This ranking wasn't compatible with our study.

Allergic reactions developing against antibiotics are the most known and most fearsome side effects of this group of medications (14). Allergic reactions developing with the use of antibiotics can be seen in different forms from simple rash to anaphylaxis. Another side effect is skin reaction. Various types of exanthematous skin reactions can occur and it must be well-assessed in which circumstances the antibiotic must be discontinued. Many antibiotics can cause hepatotoxicity but a level of toxicity in which the therapy must be terminated is not very common. The most common gastrointestinal side effect is diarrhea (14). Nephrotoxicity, hematologic side effects, cardiac side effects, autotoxicity, neurotoxicity, musculoskeletal side effects and electrolyte disorders are the other side effects.

In our study, 329 out of 353 patients (93.2%) used the antibiotics within recommended time and dose, 24 of them (6.8%) showed nonadherence. Number of patients in our study with nonadherence was significantly lower than other studies. The region of our study has a high level of income, education and HL. In a study conducted by Kukula in 2018, it was reported that, 34.6% of the participants used the antibiotics until they are finished, 26.2% of them used the antibiotic in the length of time prescribed by the physician (15). In that study, antibiotic adherence was found much lower than our study. The reason of this can be the high mean age in our sampling. Shorter recovery time of the young people can be a reason of this.

High adherence rate was significantly high in the participants without antibiotic use in insufficient time and dose and low adherence rate was significantly high in those with antibiotic use in insufficient time and

dose. In a study conducted by Yılmaz et al. in Ankara in 2016, it was found out that HL and medication knowledge affected medication adherence, as well as socio-economic factors (16). In that study, it was identified that drug nonadherence was mostly among diabetes-diagnosed patients. Patients' beliefs can play a role in their medication adherence. In the same study, it was detected that belief on the necessity of the drugs had a positive effect on medication adherence of old individuals with chronic diseases and belief on excess use had a negative effect (16).

As a result of our study, it was detected that medication adherence was significantly higher in the participants with high HL. No cases with inadequate HL were seen. There were 4 (1.1%) problematic HL, 116 (32.9%) sufficient HL and 233 (66.0%) excellent HL. In a sectional study conducted on in-patients under treatment, it was found out that awareness of the participants about Rational Drug Use and their HL level were inadequate (17). HL levels of the participants of our research were high. Region of our study had a high education and income level; briefly it was a region with features which positively contributed to HL level. In a study, it was detected that HL level of the patients applying to family physicians tend to rise with increase in education and income level (18). HL level was found higher in those who covered medicine expenses, inadequate and problematic HL was found higher in student group (18). It is observed in our study that high HL level of participants has a positive impact on antibiotic adherence.

High medication adherence has been reported in the studies conducted in primary care with chronic hypertension and diabetes cases (19, 20). It was also detected that antibiotics prescribed in primary care units where continuous care was received were used more regularly by patients. This situation can be an indicator the patients' trust on their family physicians

and it can also be associated with the severity of their complaints about which they apply to their family physicians. Our study results might have been negatively affected because questionnaires were filled in primary care units. In addition, the fact that cases without fever quit their medication more quickly can also be related to the severity of the disease they experience. Fever can be a stimulant directing the patients towards medication.

As a conclusion, antibiotic adherence is quite high in our region. HL levels of the patients are associated with their drug adherence levels. High education level in our region enabled us to study with a more conscious patient portfolio. Antibiotics recommended by the family physicians were used more regularly. Family physicians must behave more carefully about rational drug use, must have a full knowledge of the guides and must meet the requirements of modern medicine.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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