

Original Article

A public awareness study about antibiotic consumption habits and antibacterial resistance in north-eastern region of CyprusMehmet Ilktac¹, Mohamad Tamim Tarabishi¹, Pembe Ozbirtan¹, Canan Gulcan¹, Gulden Celik²¹ Faculty of Pharmacy, Eastern Mediterranean University, Famagusta, North Cyprus, Turkey² Faculty of Medicine, Bahcesehir University, Istanbul, Turkey**Abstract**

Introduction: Antibiotic resistance is a current global issue. Investigation of the level of knowledge of the public about antibiotics and antibiotic resistance is necessary to combat the antibiotic resistance problem. The aim of the present study was to evaluate the level of knowledge of the citizens of the north-eastern part of Cyprus on antibiotics and antibiotic resistance problem.

Methodology: Randomly selected 701 adults were included in the study. A modified version of World Health Organization's public awareness survey was used to assess the knowledge on antibiotics and the resistance. Logistic regression was used to find out the relationship between knowledge and education level. Spearman's correlation analysis was carried out to determine the association between the education level and the awareness of antibiotic resistance.

Results: Overall, 47.9% (336/701) of the respondents had used antibiotics in the last 6 months. Approximately 70% of respondents were determined to have intermediate/high knowledge on antibiotic consumption. In total, 66% of the population heard about antibiotic resistance and of these, 64% had intermediate knowledge on the resistance concept. University graduates were more likely to hear the term antibiotic resistance than primary school graduates.

Conclusions: In the north-eastern region of Cyprus, the public is moderately knowledgeable about antibiotics and resistance. The study is the first large scale study in the northern part of Cyprus and is thought to improve the national health policies related with antibiotic consumption in Cyprus and other developing countries.

Key words: Antibiotic; awareness; knowledge; resistance.

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Introduction

The discovery of the first antibiotic, penicillin, by Alexander Fleming in the early 20th century earned him the Nobel Prize award in physiology and medicine two decades later. Along with this discovery, a new revolution in the field of infectious diseases, that is the treatment of bacterial infections, had begun. The cascade of events initiated by Fleming's findings led to the discovery of a huge number of antibiotics and their introduction into clinical practice. During the course of seven decades after 1928, more than 30 antibiotics had been discovered and introduced into the pharmaceutical market. The events in the 20th century denoted the century as the "antibiotic era" [1].

The increase in the number of antibiotics that could be used to treat bacterial infections was obscured by the mechanisms that bacteria adapted in order to overcome the biological effects of antibiotics. These mechanisms lead to the development of antibiotic resistance that results in difficulties in the treatment of bacterial infections. As antimicrobial agents had been discovered

and introduced into clinical practice, bacteria used two major genetic strategies, mutation in the genes and acquisition of foreign resistance genes via horizontal gene transfer, in order to adapt to the antibiotic attack that eventually led to the development of resistance. Together with the shortage of the discovery of new antibacterial agents since the early 2000s and the increase in the number of bacteria becoming resistant to multiple antibiotics, the world had started to experience a serious problem because the treatment of infections was becoming difficult [2]. At the beginning, multi-drug resistant bacteria were generally isolated from hospital acquired infections. However, due to the dissemination of these microorganisms to the community and the increase in the antibiotic resistance among the bacteria isolated from community acquired infections, antibiotic resistance has become a serious risk to the public in general. Whether community or hospital acquired, antibiotic resistance not only leads to an increase in the mortality rate, but also adds to the health expenditure due to the extended hospital stay and

the attempts to eradicate the infection using different drugs. In 2014, the World Health Organization (WHO) released the first antimicrobial resistance surveillance report that contained catastrophic news as it declared that antibiotic resistance is no longer of the future but rather a present-day problem threatening the world. The report also stated that at the current rate of resistance acquisition, common infections and minor injuries could prove fatal [3]. Following the year 2014, WHO had implemented a new surveillance system known as “Global Antimicrobial Surveillance System (GLASS)” in the effort to survey the resistance and its international spread, to implement and assess intervention and control programs and to monitor their outcomes [4,5].

There are many reasons behind the drastic increase in the rate of antibiotic resistance. Irrational use and mis/over-use of antibiotics among humans, in husbandry and agriculture are among the important factors. Antibiotics, when consumed by a human, increase the frequency of mutation, a genetic mechanism which is responsible for the development of antibiotic resistance, of both the bacteria involved in the treated infection and the normal flora bacteria leading to the emergence of antibiotic resistant variants [6]. Moreover, unnecessary use or misuse of antibiotics results in selective pressure that promotes the growth and increases the pool of resistant bacteria. Once it has developed, resistance can spread among bacteria via various horizontal gene transfer mechanisms. Antibiotics not only select for resistant bacteria but also increase the frequency of horizontal gene transfer among bacteria leading to the dissemination of the resistance [7]. As a result, increased consumption of antibiotics by human not only produces resistance at the individual patient level but also produces resistance at the community, country or regional levels [8].

More than half of the antibiotics used in husbandry either for treating infections or as growth factors to promote mass gain and production are also used by humans [9]. The use of antibiotics in animal husbandry leads to the emergence of antibiotic resistant zoonotic agents which can transmit to human and cause antibiotic resistant infections. Moreover, antibiotics used in animals are excreted in their urine and faeces into the environment leading to resistance development in environmental bacteria that can also infect human. In addition, the manure produced by the livestock is frequently used as nourishment for the soil which in turn contributes to the presence of resistant bacteria in the soil [10]. Charuaud *et al.* [11] revealed that pharmaceutical residues from veterinary sources had reached concentrations up to a couple of micrograms

per litre in natural water. In addition to the emergence and selection of antibiotic resistant bacteria, the contamination of the natural water and soil with pharmaceuticals also creates an agro-ecosystem crisis [12]. The acuteness of the case and its insinuations pressurized the European Union (EU) and other countries to take action. In 2006, EU banned the use of antibiotics for the purpose of growth promotion in cattle [13].

In the north of Cyprus, the use of antibiotics had not been monitored and antibiotics were dispensed as over the counter drugs. But as of April 1, 2016, the government had decided that antibiotics would only be sold if a prescription had been presented in order to control the use of antibiotics and stop their misuse by the public. The aim of the study was to evaluate the level of awareness of antibiotic resistance among public in the eastern region of North Cyprus.

Methodology

Study Population

The minimum number of individuals that should attend the survey had been determined to be 381 by considering the population of the region as 40,920 according to the data from State Planning Organization of North Cyprus with 5% of margin of error and 95% confidence interval. Nevertheless, the interview was carried out on 701 locals so that the margin of error was reduced to 3.67%.

Survey

A questionnaire modified from the WHO was conducted on random citizens [14]. The questionnaire that was conducted face by face was divided into several sections. The first section consisted of demographic information including education, age and gender. Section two included four questions related with habits of antibiotic consumption followed by section three that consisted of four questions about general knowledge on antibiotics. The last section included 20 true/false questions related with antibiotic resistance.

The content validity was assessed by two experts from different fields (microbiologist and pharmacoeconomist). For improving the content validity, a pilot study was conducted on 35 randomly chosen respondents. The respondents were asked to fill in the questionnaire and were allowed to comment on the clarity of the questions. After the pilot study, minor amendments were done according to the comments of the participants.

The reliability of the questionnaire was confirmed by another pilot study done on 30 people. Cronbach’s alpha coefficient was used to analyse the internal consistency reliability. Cronbach’s alpha coefficient was determined to be 0.882 reflecting good consistency.

Evaluation of the Survey

Out of four questions related with the general antibiotic knowledge in section three, respondents who correctly answered three or more were determined to have high level of general knowledge, those who answered two questions correctly to have intermediate level of knowledge and those who answered one or none of the questions to have low level of knowledge. For the questions related with antibiotic resistance in section four, one point was assigned to each correct answer. Those people who scored ≥ 80%, 51-79% and ≤ 50% were regarded to have high, intermediate and low level of knowledge about antibiotic resistance, respectively.

Statistical Analysis

The data were analysed by IBM SPSS statistics version 21. Logistic regression was used to find out the relationship between knowledge and education level. Spearman’s correlation analysis was carried out to determine the association between the education level and the awareness of antibiotic resistance. Fischer’s exact test was used to determine the statistical significance. The level of statistical significance was set at $p < 0.05$.

Results

Demographical Data

In total, 359 (51.2%) men, and 342 (48.8%) women were included in the study. Of 701 participants, 32% and 23.4% were in between 25-34 and 35-44 years old, respectively. Approximately, 39% of respondents were high school and 42% were university graduates (Table 1).

Table 1. Demographical data of the participants.

Characteristics	n (%)
Gender	
Male	359 (51.2)
Female	342 (48.8)
Age group	
18-24	127 (18.1)
25-34	224 (32)
35-44	164 (23.4)
45-54	122 (17.4)
55-64	41 (5.8)
65+	23 (3.3)
Education level	
Primary school	80 (11.4)
High school	270 (38.5)
University	296 (42.2)
Master’s	51 (7.3)
PhD	4 (0.6)

Antibiotic Consumption Habits

In total, 434 (61.9%) of the participants were on antimicrobial therapy or had had the therapy in the past 12 months and 336 (47.9%) respondents had used antibiotics in the last 6 months. Majority (75.6%) of the participants reported that they buy antibiotics upon doctors’ advice. Approximately 88% of respondents replied that they adhere to the advice of the pharmacist or the doctor on how to use the antibiotics (Table 2).

60% of the interviewees responded that they requested the same antibiotic from the doctor if they suffered from the same symptoms before and the antibiotic helped. Approximately 18% of the participants replied that they used a leftover antibiotic from a family member or friend as long as it is being used for the same sickness (Table 2). 27% of the population stated that they stop using the antibiotic when the symptoms disappear.

72% of the interviewees responded that antibiotics can be used in the treatment of bladder infection where as 26.5% of the participants had misconception that antibiotics can be used in the treatment of viral infections including Human Immunodeficiency Virus (HIV). Cold/flu perplexed 22.2% of the respondents as indication for antibiotic treatment.

Table 2. Antibiotic consumption habits, n (%).

	Yes	No
Buy antibiotic with doctor’s advice	530 (75.6)	171 (24.4)
Adhere to the advice of pharmacist/doctor	614 (87.6)	87 (12.4)
Request the same antibiotic that helped recovery from the same symptoms before	415 (59.2)	286 (40.8)
Use a leftover antibiotic from a family member/friend with the same symptom	127 (18.1)	574 (81.9)

Table 3. General knowledge of antibiotics with respect to education level, n (%).

Education	Knowledge			Total
	Low	Intermediate	High	
Primary school	30 (37.5)	19 (23.8)	31 (38.8)	80
High school	75 (27.8)	74 (27.4)	121 (44.8)	270
University or higher	108 (30.5)	81 (23.1)	162 (46.4)	351
Total	213 (30.4)	174 (24.8)	314 (44.8)	701

Table 4. General knowledge of antibiotics with respect to age, n (%).

Age	Knowledge			Total
	Low	Intermediate	High	
18-24	39 (30.7)	33 (26)	55 (43.3)	127
25-34	66 (29.5)	52 (23.2)	106 (47.3)	224
35-44	53 (32.3)	41 (25)	70 (42.7)	164
45-54	31 (25.4)	32 (26.2)	59 (48.4)	122
55-64	17 (41.5)	9 (22)	15 (36.6)	41
≥ 65	7 (30.4)	7 (30.4)	9 (39.1)	23
Total	213 (30.4)	174 (24.8)	314 (44.8)	701

Table 5. Education level of respondents according to whether they have heard about resistance or not, n (%).

Education	Have you heard about the term resistance before ?		Total
	Yes	No	
Primary school	43 (53.8)	37 (46.3)	80
High school	174 (64.4)	96 (35.6)	270
University	241 (69.5)	106 (30.5)	347
PhD	4	0	4
Total	462 (65.9)	239 (34.1)	701

Table 6. Education level of respondents according to their knowledge about resistance, n (%).

	Low	Intermediate	High	Total
Primary school	1 (2.3)	33 (76.7)	9 (20.9)	43
High school	9 (5.2)	115 (66.1)	50 (28.7)	174
University	8 (3.3)	145 (60.2)	88 (36.5)	241
PhD	2 (5.0)	2 (5.0)	0	4
Total	20 (4.3)	295 (63.9)	147 (31.8)	462

General Knowledge Related with Antibiotics

The median score of the participants for the knowledge of antibiotics was calculated to be 50%. Of 701 respondents, 314 (44.8%), 174 (24.8%) and 213 (30.4%) were determined to have high, intermediate and low level of knowledge, respectively. In general, 48% of the female and 42% of the male respondents were determined to have high knowledge ($p > 0.05$). Although the university graduates and 45-54 year old respondents had the highest level of knowledge, no statistically significant difference was detected between neither knowledge and education level (Table 3) nor knowledge and age (Table 4).

Knowledge about antibiotic resistance

Approximately 66% of interviewees, of whom 228 (49.4%) were female and 234 (50.6%) were male, heard about the term “antibiotic resistance”. More than half of all age groups and 73% of 45-53 year old respondents reported that they had heard about the term ($p > 0.05$). 53.8% of primary school graduates, 64.4% of high school graduates and 69.5% of university graduates had heard about antibiotic resistance (Table 5).

Slightly more than the half (52.1%) of those who had heard about antibiotic resistance was university graduates and logistic regression revealed that the respondents who were university graduates were significantly more likely to hear the resistance when compared to primary school graduates ($p < 0.05$).

Nearly 69% of respondents who had heard the term responded that they heard it from their doctor or pharmacist. Of those who had heard the term, an overwhelming majority (90%) of the respondents replied that humans become resistant to antibiotics and they no longer work. Approximately 86% stated that experts will handle antibiotic resistance before it becomes too serious and 58.4% replied that not much can be done to stop antibiotic resistance. Surprisingly, 64.1% of the respondents thought that antibiotic resistance is only a problem for those who consume antibiotics regularly.

Of 462 people who had heard about antibiotic resistance, 20 (4.3%), 147 (31.8%) and 295 (63.9%) were found to have low, high and intermediate level of knowledge about antibiotic resistance, respectively. 31.6% of female and 32.1% of male respondents had high level of knowledge ($p > 0.05$). 36.5%, 28.7% and 20.9% of university, high school, and primary school graduates had high level of knowledge, respectively. 59.9% of those who had high knowledge were university graduates. There was a statistically

significant correlation between education level and the knowledge of resistance ($p < 0.05$) (Table 6).

Discussion

A direct correlation between antibiotic use and the rate of antibiotic resistance has been proposed. Penicillin and macrolide resistance among *Streptococcus* strains was significantly found to be correlated with antibiotic use reflecting the fact that antibiotic resistance is directly related to the antibiotic selection pressure on a national level [15,16]. European Centre for Disease Prevention and Control (ECDC) reported that third and fourth generation cephalosporin and fluoroquinolone resistance in *Escherichia coli* strains of human origin was significantly associated with the corresponding antimicrobial consumption in human. The rate of carbapenem resistance of *Klebsiella* strains isolated from humans was also linked to the antibiotic use in human. Moreover, fluoroquinolone resistance in *Salmonella* spp. and *Campylobacter* spp. from humans was reported to be due to the use of fluoroquinolones in animals [17]. Such a relationship between antibiotic consumption in animals and antibiotic resistance in human puts forward the importance of “one health” approach to antimicrobial resistance.

Antibiotics lead not only to genetic alterations on bacterial cells resulting in increased virulence but also to increased mutagenesis and horizontal gene transfer that result in the emergence and the dissemination of the resistance, respectively [18]. Thus, antibiotic consumption is one of the drivers of both the emergence of the resistance by exerting selective pressure and the dissemination of the resistance by inducing the transfer of resistance elements [19].

Both health care professionals and the public are accountable for preventing antibiotic resistance from becoming a more serious public health problem both nationwide and worldwide. Physicians should take care as they prescribe antibiotics by ensuring that patients have bacterial infection. Pharmacists should not dispense antibiotics to patients without prescription, or for viral infections, or on patient demand. Pharmacists also have the task to educate patients about the use of antibiotics and the risks associated with their misuse. Patients should avoid the overuse of the antibiotic, cessation of treatment before a full course is finished, or self-treatment. At the present, there is a shortage in the discovery of novel therapeutics or innovative mechanisms of action, thus efforts are being directed towards reducing the rate at which the issue is transpiring. Guaranteeing the right use of antibiotics is

critical to hinder the speed at which it is happening. Thus, many awareness campaigns had been carried out in order to inform the public about the risks and the right use of antibiotics. These campaigns were demonstrated to be effective for both detecting the knowledge and increasing the awareness of the public [20].

The present study, employing a customized version of WHO's awareness survey on antibiotic resistance, intended to investigate the use of antibiotics, the comprehension of the antibiotic resistance problem and the knowledge about the use of antibiotics in the northern part of Cyprus. In this study, the level of familiarity about antibiotics and resistance was found to be correlated to the level of education of the correspondents. Individuals who had higher levels of education showed better results regarding the general knowledge about antimicrobial resistance. This is in consistent with the observation that people with low level of education are more likely to consume antibiotics compared to people at a high level of education [14,21-24]. More than 90% of the people living in north-eastern region of Cyprus implied that they had used antibiotics properly and according the pharmacists instructions.

The rate of antibiotic consumption (47.9%) in the past six months was found to be lower than that (67.5%) reported globally by WHO [14]. The antibiotic consumption rate within the past year was reported to be high at the rates of around 60% in Turkey, Kosovo and Oman [22,25,26]. On the other hand, the rate of antibiotic consumption in previous twelve months was reported to be 30-38% in Italy, Germany and Poland which reflects the fact that people living in these countries, in general, have lower rate of antibiotic consumption in comparison to that reported in our study [27-29].

Only 22.2% of the respondents in our study replied that antibiotics can be used for cold and flu. The rate of misconception is comparable to that reported in Sweden and Netherland as 20% [30,31]. Similar to the present study, 25% of Iraqi undergraduate students reported that antibiotics may be required cold/flu [32]. On the other hand, the misconception about the effectiveness of antibiotics against common cold/flu and other viral infections was reported to be at higher rates of 47.8% in Netherlands, 39% in Oman, 30% in Poland, 44.8% in Turkey, 42.5% in Kosovo and 41.7% in Lithuania [21,22,25,26,28,31] and at the highest rate of 64% globally by WHO [14]. The differences in the rate of misconception in different countries may be due to the differences in the presence or absence of awareness

campaigns or in the efficacies of the campaigns implemented by local health organizations.

Approximately 18% of the Cypriot respondents replied that using a leftover antibiotic from a family or friend is appropriate as long as it is being used for the same sickness. Such a misconception was found to be higher (28%) in Germany, lower in Sweden (8%), Iraq (8%) and Turkey (10%) [25,27,30,32].

Approximately 27% of the population of our study stated that they stop the antibiotic when the symptoms regress. In a Swedish study [30], only 5% of respondents stated that stopping the antibiotics when they feel better is an appropriate habit whereas the misconception was detected to be at the rate of 53% in Oman and 14% in Iraq [22,32]. In parallel to our study, Turkish adults were frequently reported to stop using antibiotics when they feel better [33]. These data clearly denote that the Swedish people are more informed about antibiotics and their use among many European countries.

Approximately 60% and 68% of citizens in Lithuania and Senegal were demonstrated to have poor antibiotic knowledge, respectively [21,34]. In our study, only one-third of Turkish Cypriot citizens were found to have low knowledge. In consistent to the data provided by our study, Oman citizens and majority of Pakistani parents were reported to have moderate knowledge on antibiotic related aspects [22,23].

It is very important that the public is attentive and familiar with the antibiotic resistance and the public health problem that it exerts. The awareness about the antibiotic resistance changes from country to country and even varies in the different geographical regions of the same country. In a study carried out in Turkey, only 20% of Eastern Anatolian Turkish people were reported to hear about the term "antibiotic resistance" [25]. As far as 70% of Jordanian people reported that they did not hear about the resistance [24]. On the other hand, all of pharmacy students were detected to be aware of the term in Iraq [32]. In our study, a high proportion of participants (66%) heard about the term. The differences in the rate of the awareness of antibiotic resistance in the studies may be as a result of the differences in the demographical and educational differences in the populations.

90% of the respondents in our study replied that humans become resistant to antibiotics and they no longer work. Such a misconception was obvious among the majority of respondents in studies carried out in Italy (70%), Sweden (84.7%), Germany (71.3%), in the WHO global report study (76%) and among pharmacy students in Iraq (69%) [14,27-30,32]. In parallel to the

studies carried out in Italy and Iraq, approximately 90% of the respondents included in our study were aware that many bacterial infections are becoming resistant to antibiotics [29,32].

Conclusion

Infections caused by antibiotic resistant bacteria have still been common public health problem all over the world and to increase the public awareness is one of the most important step in order to reduce the misuse of antibiotics, a habit that increases the emergence of antibiotic resistant bacteria. Although, as a limitation, the number of questions is low, the present study revealed that the public is moderately knowledgeable about antibiotics and antibiotic resistance. The results of the present study that involved a subset of population from the north-eastern region of Cyprus may not be generalized to all over the country. However, due to the new laws regarding the dispensation of antibiotics, this study could be a stepping stone for the health regulation in northern part of Cyprus. According to our knowledge, there has been no earlier large-scale antibiotic resistance awareness study conducted in the region and the study highlights the importance of awareness studies carried out in developing countries since the majority of the people were determined to have intermediate level of knowledge about antibiotic consumption and the resistance. The study possibly has the characteristic to be the foundation onto which further studies will be performed in order to find out the habits of antibiotic consumption, the knowledge of antibiotic resistance amongst the public and to advance the national health policies in developing countries.

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