



Prevalence Study of Antibiotic Usage and Health Care Associated Infections in Northern Cyprus

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Authors' contributions

This work was carried out in collaboration between all authors. Author WJ was responsible for design and implementation of study. Author WJ finalized study design and coordinated implementation. Authors AMA and HKS were collected data. Author BB carried out statistical analysis. Authors WJ and AMA carried out data interpretation and creation of the manuscript. Authors BB and NC supervised, reviewed and improved the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Purpose: This study aims to provide a prevalence survey of antibiotic usage and HAIs and evaluate the cost of antibiotic therapy.

Methods: All inpatients on surgery, paediatrics, medicine, and ICU specialities were surveyed within a period of one week, April 2016 at Near East University hospital in Northern Cyprus. A cross-sectional study was performed and desired data on antibiotic use and HAIs were collected and analysed.

Results: Out of 137 inpatients, 39.4% (n=54) were on one or two antibiotics. The usage of antibiotic was appropriate in 70% of the patients while it was inappropriate in the remaining 30%. The most common appropriate use was seen in empirical (80.6%) and prophylaxis (69.2%), while in definitive therapy cases (60.0%), the usage of antibiotics was irrationally inappropriate. Overall,

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10.9% of hospitalized patients developed HAI. The most prevalent infection was UTI (urinary tract infections) (33.3%). Prevalence of HAIs was high in patients over 30 years old and in those who stay in hospital more than 10 days. The overall daily cost of antibiotic therapy was \$919.61 per day, while the total daily cost for hospital infections was \$482.

Conclusion: Irrational antibiotic use was seen mostly in definitive therapy, continuous use of empirical therapy without carrying microbiological test was commonly observed. The prevalence of HAI was relatively high which led to more hospitalization and more cost.

Keywords: Antibiotic; prevalence; hospital acquired infection; rational use.

1. INTRODUCTION

Antibiotics as much effective they are in controlling infectious diseases and achieving a cure or disease prevention, still they are among the drugs associated with the highest costs worldwide and account for about one fourth of total drug expenditures [1]. As many developing countries deem a proper healthcare surveillance systems and strict regulations to avoid irrational use of antibiotics which ultimately lead to the increase of bacterial resistance and other adverse clinical and economic consequences, the lack of surveillance will lead to underestimation of such major gaps in healthcare systems [2]. In Turkey, where more proper healthcare surveillance systems exist, the total expenditure on antimicrobials were estimated to be 13.9% of all drug costs and ranked first in general drug expenditures though the majority of this consumption is considered irrational [3,4]. Prevalence surveys are considered as a useful tool for measuring and monitoring the burden of HAI and antimicrobial usage rate [5]. Hospital-acquired infections or more appropriately health care-associated infections (HAI) are by far the most common complications affecting hospitalized patients and greatly cause mortality and morbidity [6]. A specified number of outcomes of a population can be measured by prevalence survey at a specific period of time. The period of time may last for a week, month or season. The main objective of this study is to estimate the usage of antibiotics, both appropriate and inappropriate usage, and determine the prevalence of hospital acquired infections HAIs in an educational hospital in North Cyprus.

2. METHODS

A cross-sectional survey of antibiotic usage and health care associated infections was carried out for a period of one week in April, 2016. The study was done by reviewing electronic records of hospitalized patients, informal interviews of

treating clinicians and patients, and scanning of laboratory records. Patients on surgery, medicine, pediatrics and intensive care unit (ICU) wards at Near East University hospital were included. The medicine ward involves endocrinology patients, geriatrics, gynecology, Infectious disease, respiratory and allergy, cardiology, gastrointestinal (GIT), orthopedic and urology department's patients.

2.1 Sampling and Time Window

All inpatients who received an antibiotic are scanned for Period prevalence survey (PPS) between the 11th and 18th of April 2016 as a 1 week period survey without randomization.

2.2 Inclusion Criteria

All hospitalized patients of any age using antibiotics were eligible for inclusion and also patients that were temporarily absent from the wards e.g. (for endoscopy, surgery, medical imaging) were scanned; only patients on systemic antibiotics were included in this study.

2.3 Exclusion Criteria

All patients in an outpatient area (including hemodialysis patients) and psychiatric, neurology, oncology, ophthalmology, ear, nose and throat (ENT), rehabilitation and emergency units were excluded; also patient using topical antibiotics were excluded.

2.4 Data Collection

Necessary data was taken from computerized records during the study and by reviewing patient's records at each clinic. Demographic information on the patients was collected in the first part of the survey e.g. (gender, age, name of the ward where the patient was treated, date of hospital admission, etc) while the second part collected information about antibiotics for example, antibiotic usage indication, generic name of antimicrobial agent used, starting date

of using antibiotics, dose frequency, route of administration, dosage form. Also laboratory and culture results were gathered to determine whether antibiotics were used for empirical, prophylaxis or definitive therapy. The last part was about hospital acquired infections (HAIs) which included data on microorganisms and only results that were available on the time of the survey. Age of the patient, date of hospital admission, date of starting antibiotics and length of hospital stay, were used to estimate the total number of health care associated infections.

2.5 Case Definitions

Case definitions that were developed by the United States Center for Disease Control and Prevention (CDC) were used. We considered that an active infection is called a healthcare-associated infection (associated to acute care hospital stay only) when it meets the following criteria:

1. If the signs and symptoms started on day 3 of the current admission or later (with day 1 being the day of admission) and it was not present or incubating at the time of admission.
2. Antibiotics treatment was continued on the day of the survey.

The HAI was classified as lower respiratory tract infection, surgical wound, urinary tract infection, skin and soft-tissue infections, bloodstream, catheter related infection and others.

An antibiotic appropriateness was estimated by using the Council for Appropriate and Rational Antibiotic Therapy (CARAT) criteria [4]. These criteria included requirements to rationalize the use of antibiotics such as evidence-based results, therapeutic benefits, optimal drug,

optimal duration, safety and cost-effectiveness. The CDC guidelines on antimicrobial use were also used as references to the appropriate therapeutic recommendations and the cost of antibiotic therapy was calculated in United States (US) dollars.

2.6 Data Analysis

Privacy of patient's data was assured by using a code system. All data were analyzed using the Statistical Package for Social Sciences software (SPSS version 22).

The data were described using frequency distributions. Categorical variables were analyzed by Chi-square test and statistical significance was accepted when the chance for confidence was less than 1%.

3. RESULTS

On the time of prevalence study, the total number of hospitalized patients was 137. The percentage of patients on surgery, medical, pediatric and ICU wards was 23(16.8%), 86(62.8%), 16(11.7%), 12(8.8%), respectively. Of 137 inpatients, 54 (39.4%) were on one or two antibiotics. Among patients receiving antibiotics, 7 were in surgery ward, 35 were in medical ward, 6 in pediatric ward and 6 in ICU unit. The prevalence of an antibiotic use according to specialty and gender is summarized in Table 1.

We do not find a significant difference in antibiotic use between specialty and gender. Of 54 patients on antibiotics (90.7%) were using one antibiotic and (9.2%) were using two antibiotics. The appropriateness of an antibiotic use according to specialty and indication are given below in Table 2, the indications of using an

Table 1. Prevalence of antibiotic use by specialty and gender

Specialty	Total surveyed patient		Patient on an antibiotic use	
	N	%	N	%
Surgery	23	16.7	7	30.4
Medicine	86	62.7	35	40.7
Paediatric	16	11.6	6	37.5
ICU	12	8.7	6	50.0
Total	137	100	54	39.4
Gender				
Male	69	50.3	27	39.1
Female	68	50.3	27	39.1
Total	137	100	54	39.4
Shown by row percentage				

Antibiotic were evaluated by using criteria of empirical, prophylaxis and definitive therapy. It was found that the most common indication of using antibiotics was empirical (57.4%) while 24.1% and 18.5% were prophylaxis and definitive therapy respectively.

Table 2. Appropriateness of antibiotic use according to specialty and indication

Specialty	Appropriateness		Inappropriateness		Total	
	N	%	N	%	N	%
Surgery	7	100	0	0	7	100
Medicine	22	62.8	13	37.1	35	100
Paediatric	4	66.7	2	33.3	6	100
ICU	5	83.3	1	16.7	6	100
Total	38	70.4	16	29.6	54	100
Indication						
Empiric	25	80.6	6	19.4	31	100
Prophylaxis	9	69.2	4	30.8	13	100
Definitive	4	40.0	6	60.0	10	100
Total	38	70.4	16	29.6	54	100

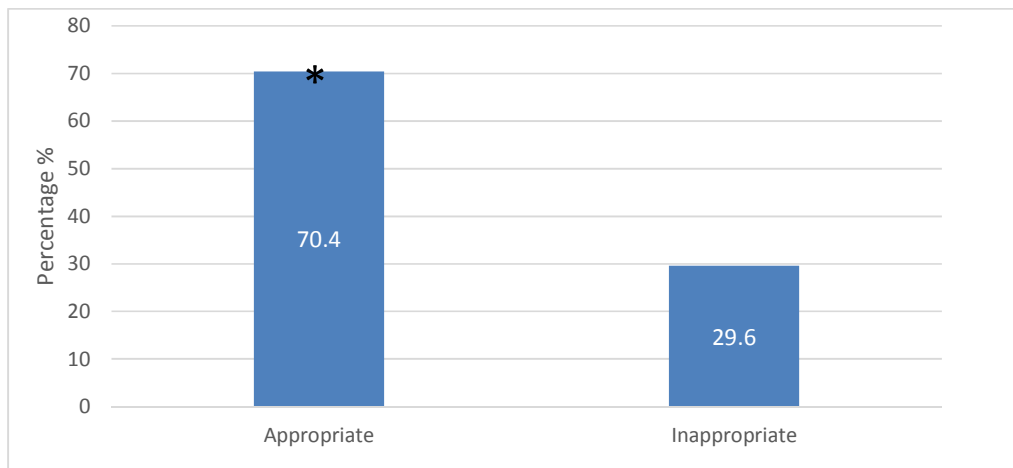


Fig. 1. Rationality of antibiotics

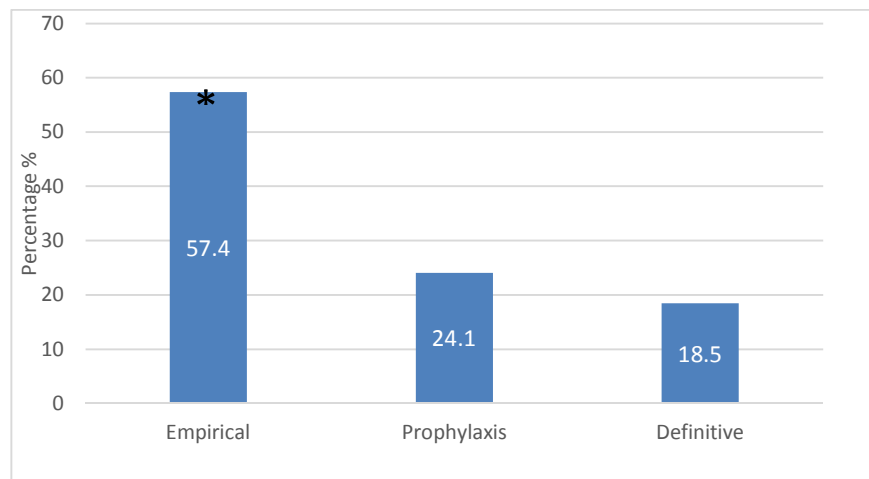


Fig. 2. Indications of antibiotics

At the time of analyzing the appropriate use of an antibiotic according to indication, it was found that, the most common appropriate use was empirical (80.6%) and prophylaxis (69.2%) while the most common incidence with inappropriate antibiotic use was those indicated for definitive therapy (60.0%). Appropriate use of an antibiotics (70.4%) was significantly ($P < 0.01$) higher than inappropriate use (29.6%) as shown in Fig. 1.

Fig. 2 also, observed that empirical therapy was significantly higher than prophylaxis ($P < 0.01$).

Antibiotics were given via two main routes, intravenous IV (88.9%) and oral rout (11.1%). During the study period, 59 antibiotics were used by 54 hospitalized patients. The distribution of antibiotics by group is summarized in Table 3.

Table 3. Distribution of antibiotics by groups

Antibiotics	N	%
Cephalosporins	29	49.2
Cefazoline	17	
Cefuroxime	3	
Ceftriaxone	8	
Cefixime	1	
Betalactams+Betalactamase inhibitors	13	22.0
Amoxicillin+ Clavulanic acid	6	
Tazobactam + piperacillin	5	
Ampicillin	2	
Macrolides	2	3.4
Clarithromycin		
Carbapenems	1	1.7
Meropenem		

Based on the group, the most commonly used antibiotic was Cephalosporin (49.2%) and according to the preparation, the most commonly

prescribed antibiotics were Cefazoline (28,8%), Ceftriaxone (13,55%), Amoxicillin + Clavulanic acid (10,2%) and Tazobactam + Piperacillin (10,0%). Antibiotic used for prophylaxis and empirical therapy belonged mainly to Cephalosporin group (92.3%). The most preferred antibiotic for definitive therapy was from Beta-lactam group (23.1%). Table 4 explains types of clinical diagnosis for 41 patients in the period of study.

Table 4. Type of infections for which antibiotics was prescribed

Type of infections	N	%
Upper respiratory tract infection	5	12.8
Lower respiratory tract infection	5	12.8
Blood stream infections	4	10.3
Urinary tract infections	13	33.3
Skin and soft tissue infection	1	2.6
Prosthesis	1	2.6
Meningitis	2	5.1
Appendicitis	1	2.6
Others	9	21.9
Total	41	100

Of those 41 patients; 15 had hospital acquired infections. The most prevalent infection was Urinary tract infection (33.3%). The overall cost of antibiotic therapy in one day in the center of study was \$919.61; the main daily cost per patient was \$17.02. The main daily cost per patient was \$8.12 in surgical wards, \$21.57 in medical wards, \$6.94 in pediatrics and \$5.79 in ICU ward. The overall, 10.9% of hospitalized patients with hospital acquired infections, ranged from 12.8% in medical to 33% in intensive care unit. The prevalence of hospital acquired infection by age group and length of hospital stay is summarized in Table 5.

Table 5. Prevalence of HAIs by gender, age groups and length of hospital stay

		Total patients	HALs	%
$\rho = 0.1$	Gender			
	Male	69	10	14.5
	Female	68	5	7.4
$\rho = 0.001$	Age group*			
	< 30 years	54	0	0
	>30 years	83	15	18.7
$\rho = 0.00$	Length of hospital stay*			
	3 – 6 days	61	0	0
	6 – 10 days	49	0	0
	>10 days	27	15	55.6
	Total	137	15	100
Shown by row percentage				

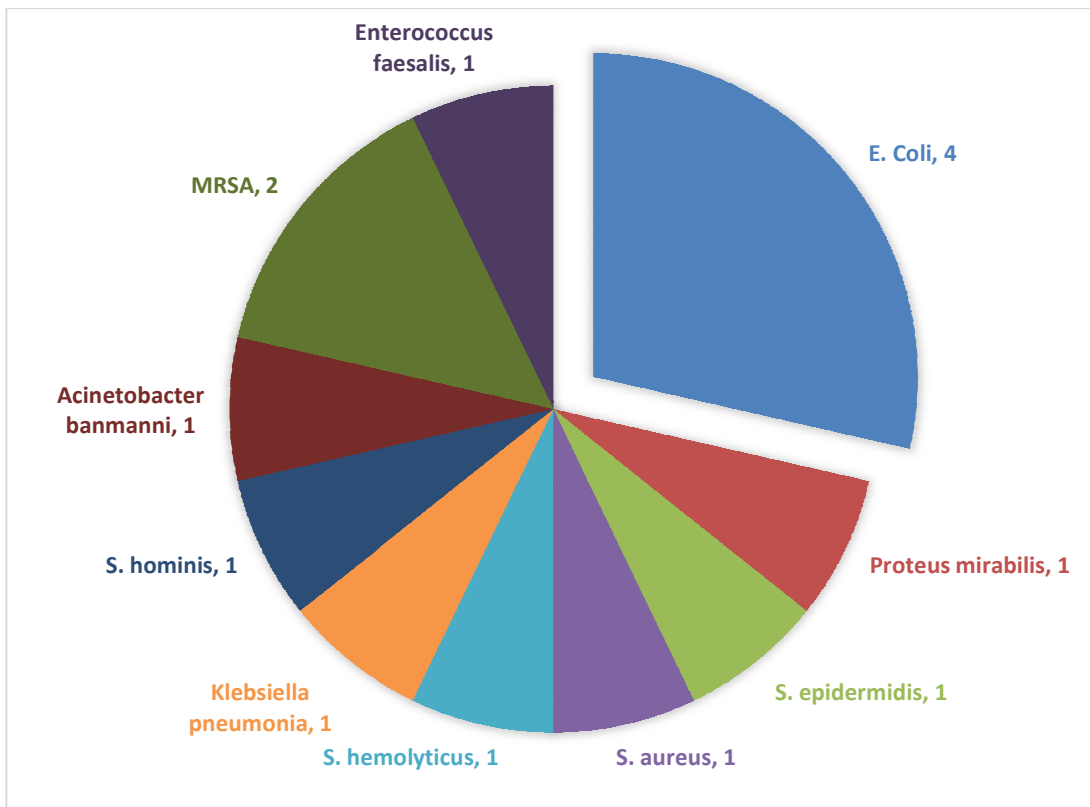


Fig. 3. Number of isolated bacteria in nosocomial patients

The two variables (age and hospital stay) were significantly related to HAIs ($P < 0.01$). Patients aged above 30 years (PR: 18.07%, $P = 0.001$) and patients who had spent more than 10 days in the hospital since admission (PR: 55.6%, $P = 0.000$) were more likely to have hospital acquired infection compared to younger patients with shorter stay in the hospital. We did not find any statistical significant regarding the relation between HAIs and gender ($p = 0.1$). In Fig. 3, it is obvious that the most commonly isolated type of bacteria was *Escherichia coli* (26.7%).

The percentage of *Methicillin resistance staphylococcus aurous* was 13.3%. The most prevalent isolated type of bacteria in patients with nosocomial infections was *Staphylococcus species*. The total daily cost of management of nosocomial infections was \$482 and the main daily cost per patient with hospital infections was \$32.13.

4. DISCUSSION

One of the most considerable roles to establish a good, cost-effective health care system is to rationalize the use of antibiotics in the hospital

and adopt effective monitoring procedures to assure rationality. Since our study center provides a service for approximately 40% of the population of Northern Cyprus, this study may reflect the current antibiotics use practice in Northern Cyprus hospitals. The main purposes of using antibiotics are empirical, prophylaxis and definitive therapy. According to the results of various prevalence studies performed in Turkey and worldwide [7,8,9,10], antibiotics usage rate varied between (36.2%) to (67.4%). In our study (39.4%) of the inpatients were receiving antibiotics. It demonstrated that the antibiotic usage rate was relatively low. In a similar way, the inappropriate usage rate of this study was (29.6%), it is considered low when compared with the results that were reported on the previously mentioned studies that varied from (30.8%) to (68.8%). In assessing practices leading to inappropriate use of antibiotics, the most common reasons reported on studies were unnecessary prolonged use of prophylaxis therapy and empirical therapy, in a similar way our findings (60%) of inappropriate usage was due improper choice of antibiotic after getting the AST and (30.8%) was from prolonged use of broad spectrum antibiotics for prophylaxis

purpose. In a study that utilized 1,966 patients in 21 European nations [11] the most common reason for antibiotic uses was empirical in (54.4%) of the cases and prophylaxis in (28.8%) of the cases. Also in this survey, empirical (57.4%) and prophylaxis (24.1%) were observed to be the most prevalent cause of antibiotic use though relatively higher percentages were seen regarding the empirical therapy compared to other European facilities. In our study it also observed that the majority of empirical therapy prescriptions were started without concomitant microbiological investigations. The overall daily cost of antibiotic therapy in this hospital was reported as \$919.61, while the main daily cost of antibiotic per patient was \$17.02. These findings are relatively higher than that reported by (Naz et al.) which found out that the main daily antibiotic cost per patient was \$13.8 and main daily antibiotic cost for hospital infection was \$25 [12]. In fact, the accurate antibiotic therapy costs were affected by various factors. For example, excessive use of intravenous administration, monitoring antibiotic adverse effects and nursing services. Thus, we suppose that the actual cost of antibiotic therapy is higher than the cost that was reported in these studies. One considerable observation in this study was that high percentage of patients was on IV antibiotics therapy(88.9%) as compared to oral rout which is 3 times costly than oral dosage form. In our survey, we used CDC standardized definitions to record data onto HAIs. The data onto onset of infection was recorded in this study to determine which infection could be classified as hospital acquired infection and according to that, it was possible to detect whether the HAIs were due long stay in the hospital or not. In our study overall prevalence of HAIs was 10.9%. Our result was considered in a medium range when compared with the results that ranged between 8% and 19.1%, for studies that performed by Pujate et al. [13] and Ider BE et al. [14]. The most prevalent HAI was urinary tract infection UTI (33.3%), a result lower than the one reported by (Theodora, AA) and his colleagues that reported UTI infections as being 48.2% [15]. Prevalence of HAIs was high in patients aged over 30 years old and in those in hospital for longer than 10 days. We consider that elderly patients are more sensitive to HAIs. The most common prevalent type of bacteria that was isolated from patients with nosocomial infections was *staphylococcus species* and our results were consistent with a finding in a study performed by Rachid Razine, et al. [16].

5. CONCLUSION

The study showed that the rate of inappropriate antibiotic uses in our hospital was low when compared with other studies. Antibiotic usage rates which were reported in this study were relatively low, this may be due to the low number of total hospitalized patients. Definitive therapy is still a major problem, so infectious disease specialist agreement and implementing a restriction policy is efficient for appropriate use of antibiotics. Also, widely use of broad spectrum antibiotics as empirical therapy without culture results to guide therapy was determined in this study. The prevalence of HAI was relatively high in the Near East University hospital as a private hospital and such infections are an important precursor for extra costs.

6. RECOMMENDATIONS

This study was the first of its kind in North Cyprus, and it's supposed to be of value for healthcare providers and regulatory bodies to aid in evaluating antibiotics usage and assure rational use of antibiotics in hospitals in Northern Cyprus.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Confidentiality was assured during the study and also patient's privacy, ethical approval for this study was obtained from the institutional review board (IRB) from Near East university hospital (Ref YDU/2015/35-263). Only initials were used during the study without recording patients address or other related not clinical important personal information. Research was conducted with the declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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