Original Research Article

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

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. ACross-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, 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.

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 (2). 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 gabs 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(1). 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.

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.

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.

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.

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.

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, rout 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 onto microorganisms and only results that 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 infection.

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.

Data Analysis: Privacy of patient's data was assured by using a cod 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%.

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.

Table 1: Prevalence of antibiotic use by specialty and gender.

	Total surveyed patient		Patient on an antibiotic use	
Specialty	**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			

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 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.

	Appropriateness		Inappropriateness		Total	
Specialty	**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**

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 figure 1.

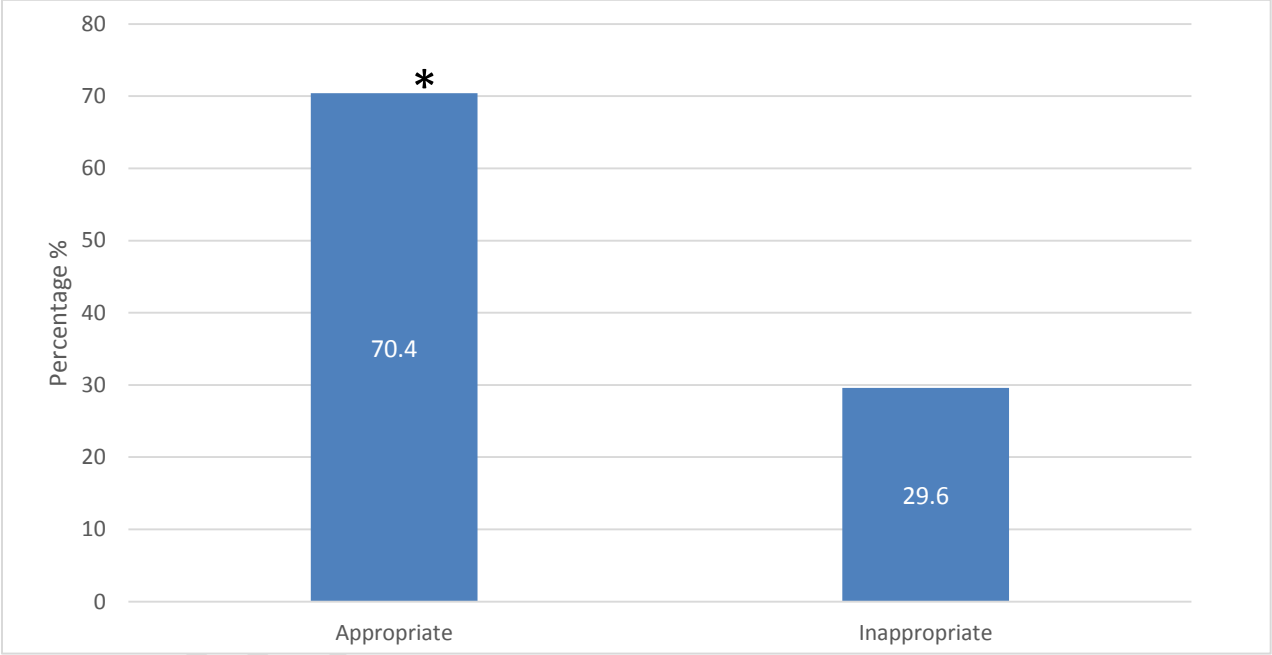

Figure 1: Rationality of antibiotics

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

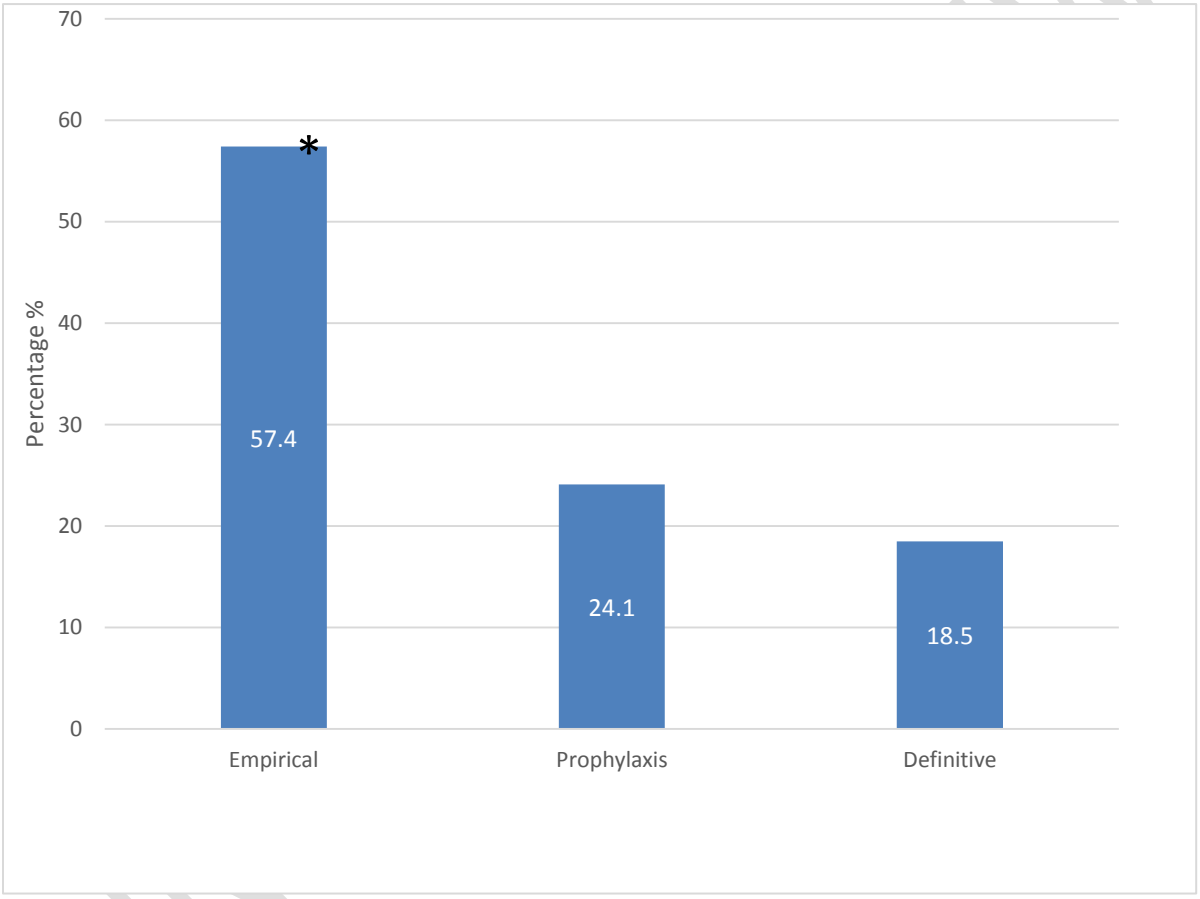

Figure 2: Indications of antibiotics

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 Clarithromycin	2	3.4
Carbapenems Meropenem	1	1.7

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

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 figure 3, it is obvious that the most commonly isolated type of bacteria was *Escherichia coli* (26.7%).

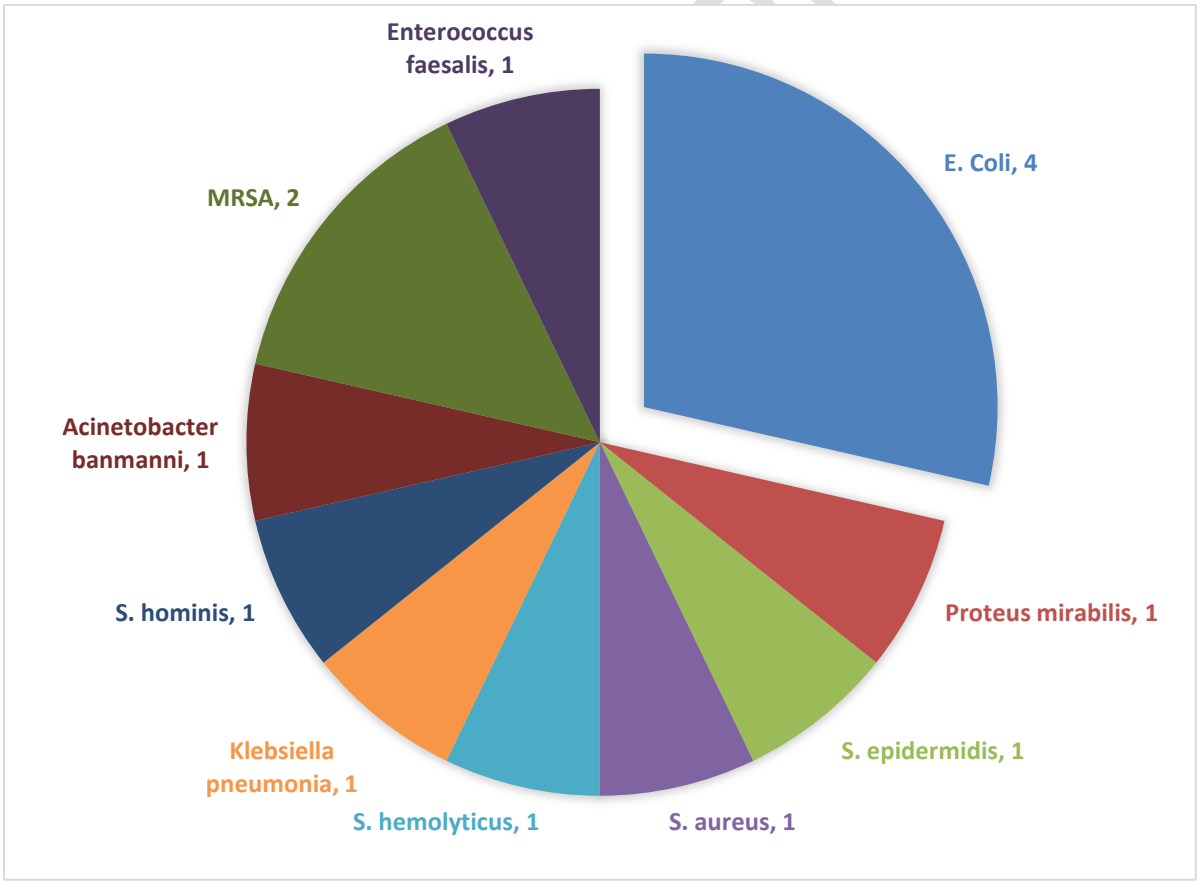

Figure3: Number of isolated bacteria in nosocomial patients

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.

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*) and (Ider BE *et al*) (13, 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 (RachidRazine, *et al*) (16).

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.

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.

Competing of interest:

The authors declare that they have no competing interests.

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