



Measurement and Comparison of Inpatient Antibiotic Use in Five Different Hospitals in Tabriz

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ABSTRACT

Background: There is a relation between amounts of antibiotic uses and creation of resistant bacteria. Due to the critical role of antibiotics and increasing trend of resistance in developing countries, comprehensive methods of antibiotic use is necessary to limit the threat of resistant microorganisms. In this study we compare antibiotics consumption by Defined Daily Dose (DDD) per 100 bed-days in teaching and private hospitals during six months in Tabriz, Iran.

Methods: Four university hospitals and one private hospital were included in this study. Amount of their antibiotic consumption obtained from the hospital pharmacies. Anatomical Therapeutic Chemical (ATC) code J01 was explained as defined daily doses per 100 bed-days (DDD/100) according to the ATC/DDD classification. The amount of consumption was assessed with DDD per 100 bed-days in six months.

Results: Total antibacterial consumption was higher in Emam reza (119.62 DDD/100) than other hospitals. Cephalosporins were the most widely used antibiotic in all five hospitals with the total DDD per 100 bed-days of 53.74, 58.51, 46.09, 19.75 and 15.16 for Emam reza, Shohada, Sina, Shahriar and Shahid madani ,respectively. Cefazoline had highest use among cephalosporins consumption in all hospitals except Shahriar. Ciprofloxacin was among the five most used antibiotics in all hospitals.

Conclusion: Although the pattern of antibacterial consumption was almost logical in different categories of hospitals, the total amount of DDD per 100 bed-days was dramatically more than developed countries. Specific strategies should be employed in infection control development and engage rational antibiotic utilization in order to reduce future resistant strains and increase antimicrobial efficacy.

Introduction

It is obvious that the total amounts of antibiotic uses are risk factors for the formation of resistant bacteria.¹ Gram-negative bacilli and Gram-positive bacteria are the most common important reasons of hospital-acquired infections.^{2,3} Antimicrobial resistance effects patient outcome in hospital and the allocation of resources.⁴ In many patients, there are few effective antimicrobial agents, particularly against resistant microbial strains.⁵

In most of the Middle Eastern countries, antibiotics are easily accessible over the counter. Inappropriate use and administration of antibiotics has led to the development of microbial resistance in Middle East. Moreover, the unreasonable use of

antibiotics is not limited to human. Antibiotics are overused and abused in veterinary medicine, poultry, and fishery industries, which develop the resistant microbial strains. These resistant microorganisms are spread to people through the food.⁶ Regarding the critical role of antibiotics and increasing trend of resistant microbial strains, particularly in Middle East, comprehensive quantitative and qualitative method of antibiotic consumption is necessary.^{7,8}

Anatomical Therapeutic Chemical (ATC) classification system is the most extensively used classification system for expression of drug utilization.⁹ The ATC system is coordinated by the World Health Organization (WHO) Collaborating

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Centre for Drug Statistics Methodology now. Based on the ATC system, drugs are separated into different groups on which they act and/or their chemical characteristics and therapeutic effect. Accordingly, each specific drug is categorized into groups at five different levels and is determined at least one ATC code. Defined Daily Dose (DDD) is designed to compare drug consumption information across time and geography. The DDD is the supposed average maintenance dose per day for the drug's main indication in adults. For different drug formulations (i.e., parenteral versus oral), different DDDs are determined.¹⁰ In addition, drug utilization is expressed with rate. Common units for antibiotic consumption rate can be defined by DDD per 100 bed-days in hospitals.⁹

Anasari *et al.* showed 101.92 DDD/100Bed days for systemic antibiotics in six months in bouali hospital in Tehran.¹¹ Previous study showed that ceftriaxone consumption was higher than other pediatric centers in Iran.¹² In addition, Mousavi *et al.* demonstrated that only 8% and 26% of empiric imipenem and intravenous Ciprofloxacin administration were consistent with American Hospital Formulary System (AHFS) mentioned indication a teaching hospital in Zabol, Iran.

In this study we compare antibiotics consumption in different categories of teaching and private hospitals during six months in Tabriz, Iran.¹³

Methods

Four university hospitals and one private hospital were included after evaluation of antibiotic use data obtained from the hospital pharmacies. The study was preformed from April to September (six months) of 2014 in Tabriz, Iran. Antibiotic use for ATC code J01 was expressed as defined daily doses per 100 bed-days (DDD/100) according to the ATC/DDD classification.

In order to determine the DDD conversion factor, the usual dose per gram of each drug is divided to its ATC/DDD amount. Multiplication of the quantity dispensed by a conversion factor equals a total of DDDs for each drug (equation 1).

$$\text{Total of DDDs for each drug} = \frac{\text{Usual dose}}{\text{ATC/DDD}} \times \text{Quantity dispensed} \quad \text{Eq.(1)}$$

For Calculation of DDD per 100 bed-days (DDD/100), total amount of each drug dispensed based on DDD is divided into bed day and multiply by 100 (equation 2). It should be mentioned that, bed day is calculated by multiplying the total number of patients in each period by number of days in that period (equation 2).⁹

$$\text{DDD per 100 bed - days} = \frac{\text{Total of DDDs for each drug}}{\text{Bed day}} \times 100 \quad \text{Eq.(2)}$$

All characteristics and information about studied hospitals is mentioned in Table 1.

Results

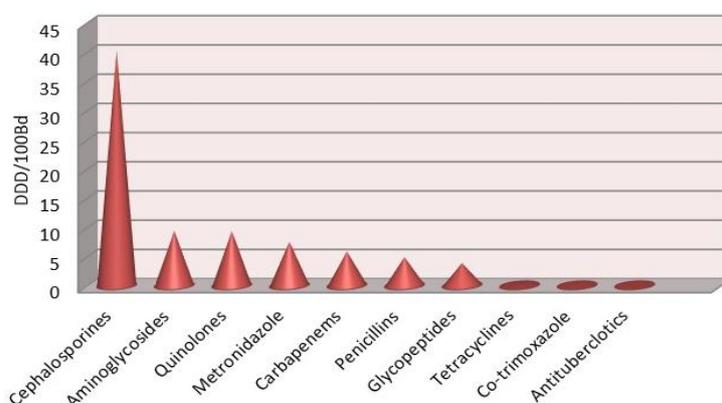
Inpatient antibiotic use and route of administration differed in each hospital (Table 1 and 2). In addition, Table 1 shows the proportion of different types of systemic antibiotics consumption according to the ATC classification for 5 hospitals. Our results showed that, total antibiotic consumption were higher in Emam reza in compare with other hospitals (Table 2). Cephalosporins (ATC group J01DA) were the most widely used antibiotics in all five hospitals with the total DDD per 100 bed-days of 53.74, 58.51, 46.09, 19.75 and 15.16 for Emam reza, Shohada, Sina, Shahriar and Shahid madani ,respectively. The old first-generation cephalosporin (cefazoline, ATC group J01DB04) still represented the highest consumption of the total inpatient cephalosporin use in all hospitals except Shahriar. In all five hospitals, we noted a very high consumption of third-generation cephalosporin (ceftriaxone, ATC group J01DD04). Ciprofloxacin (ATC group J01MA02) was included in five most used antibiotics in all five hospitals with the highest rate of 18.24 DDD per 100 bed-days in Emam reza and the lowest rate of 2.04 DDD per 100 bed-days in Shphada hospital. The highest and lowest DDD per 100 bed-days for carbapenems was reported in Emam reza and Shohada hospital (9.9 and 2.46 DDD/100, respectively). Moreover, vancomycin (ATC group J01XA01) consumption was highest in Shahid madani hospital (5.84 DDD/100) followed by Emam reza hospital (5.78 DDD/100). Total inpatient antibiotics (with different antibiotic classes) use in all five hospital is classified in Figure 1.

Table 1. Characteristics and information of studied hospitals in Tabriz (2014).

Hospital	Type	Specialty	Bed day in 6 months period	Intravenous antibiotics DDD/100BD (%)	Oral antibiotics DDD/100BD (%)
Emam Reza	University	General	82144	103.01 (86.1)	16.61 (13.9)
Shohada	University	Orthopedic	38457	86.92 (96.4)	3.25 (3.6)
Shahid Madani	University	Cardiology and Heart surgery	37232	43.8 (85.5)	7.41 (14.5)
Sina	University	General	29456	86.74 (87)	12.94 (13)
Shahriar	Private	General	12530	70.3 (91.57)	6.47 (8.43)

Table 2. Utilization pattern for ATC code J01 antibiotics in all studied hospitals in Tabriz (2014).

Class	Available anti-infectives	ATC code	Use (DDD/100 BD)				
			Emam Reza	Shohada	Shahid Madani	Sina	Shahriar
Tetracyclines	Doxycycline	J01AA02	0.22	0	0	0.2	0.03
	Tetracycline	J01AA07	0.06	0	0	0	0.28
Amphenicols	Chloramphenicol	J01BA01	0	0	0	0	0
Penicillins whit extended spectrum	Amoxicillin	J01CA04	2.32	0.14	0.11	0.46	0.82
	Ampicillin	J01CA01	2.55	0.05	1.62	6.54	1.16
	piperacillin	J01CA12	0	0	0	0.35	0
Beta-lactam-sensitive penicillines	Penicillin V	J01CE01	0	0	0	0	0
	Penicillin G	J01CE01	1.51	2.07	0	0.7	3.98
Beta-lactam-resistant penicillines	Cloxacillin	J01CF02	0.02	0	0	0	0.017
Carbapenems	Imipenem	J01DH51	3.83	1.17	1.6	4.98	0.91
	Meropenem	J01DH02	6.07	1.29	3.12	1.28	4.97
Cephalosporins	Cefazoline	J01DB04	22.2	48.8	15.16	19.89	5.5
	Cephalexin	J01DB01	1.45	0.94	0.54	0.08	0.6
	Cefuroxime	J01DC02	0	0	0	0	0
	Cefexim	J01DD08	2.37	0.29	0.83	2.9	1.28
	Cefotaxim	J01DD01	0.39	0	0	0.01	0.006
	Ceftazidim	J01DD02	7.33	6.85	0.78	2.65	2.44
	Ceftizoxim	J01DD07	0.14	0.04	0	0.06	0.25
	Ceftriaxone	J01DD04	16.15	1.01	5.55	17.78	7.4
	Cefepime	J01DE01	3.71	0.58	0.47	2.72	2.27
	Cotrimoxazole	J01EE01	0	0.01	0.02	0.28	0.04
Macrolides	Azithromycin	J01FA10	1.74	0.73	2.64	1.83	0.53
	Erythromycin	J01FA01	0.6	0.1	0	4.03	0
	Clarithromycin	J01FA09	0.18	0	0	0	0.17
	Clindamycin	J01FF01	7.92	1.07	0.95	4	4.14
Aminoglycosides	Amikacin	J01GB06	1.007	0.61	0.73	0.45	1.35
	Gentamycin	J01GB03	2.97	20.26	1.79	0	17.6
	Streptomycin	J01GA01	0.02	0	0	0.04	0
Quinolones	Ciprofloxacin	J01MA02	18.24	2.04	9.08	7.19	10.05
	Ofloxacin	J01MA01	0	0	0	0	0.09
Imidazole derivatives	Metronidazole	J01XD01	10.85	0.52	0.38	17.21	8.6
Glycopeptides	Vancomycine	J01XA01	5.78	1.5	5.84	4.05	2.14
General anti-infectives for systemic use (J)			119.62	90.17	51.21	99.68	76.77

**Figure 1.** Total inpatient antibiotics (with different classes of antibiotics) use in all five hospitals in Tabriz (2014).

Discussion

Presentation of data for antibiotic consumption in DDDs might not adequately show dosage and length of treatment differences for specific antibiotics classes between hospitals. However, Monnet and colleagues demonstrated that the number of DDD correctly illustrates antimicrobial prescriptions number for outpatients at the national level.¹⁴ Subsequently DDD number is an appropriate measurement unit to express antimicrobial use and criteria for level of antimicrobial consumption. In this study, data from five hospitals were gathered from pharmacies, and recalculate the amount of antibiotic linking to DDD. Our results showed that, total uses of antibacterial agents was higher in Emam reza, Shohada, and Sina hospital in comparison with mean value of DDD amount in five hospitals. High level of cefazolin administration as a surgery prophylaxis is reasonable in Shohada hospital which is an orthopedic center with lots of orthopedic surgeries. The amount of vancomycin's DDD is high in Shahid madani hospital, because it is referral center of cardiovascular diseases and surgeries. Not only vancomycin is used for surgery prophylaxis, it is also used for post cardiac surgeries infections. Shahriar is a general hospital with a different pattern of antibacterial usage. This can be explained by different type of patients and also limited surgery in comparison with Emam reza and Sina. In addition, Shahriar is a private hospital and the antibiotics administrations are less restricted. Both Emam reza and Sina are general university hospitals, so the pattern of antibacterial use is similar. Because Emam reza is the biggest referral center in North West of country with multiple wards it is reasonable to show the highest amount of DDD in comparison with four other hospitals. The total inpatient antibiotic use in Emam reza is almost similar with other hospitals all over the country with a majority of injectable form of drugs.^{15,16} one study which was performed in Serbia showed a higher rate than Emam reza for antibiotic use.¹⁷ It should be noted that, the antibiotics consumption is remarkably lower in European countries.¹⁸⁻²⁰ Moreover, Habibzadeh explained the different reasons for illogical antibiotics administration and consumption in Middle East countries.⁶ Drug utilization evaluation studies showed that, antibacterial consumption is not logical in developing countries. Inappropriate use of antibacterial agents leads to rising of antibiotics resistant rate. As a result, it is very important to determine effective strategies in order to standardize the antibiotics consumption. One way to define amount of optimal use is routine documentation and consumption measurement in order to report prescribers and policy-makers. It helps to have comprehensive information about

amount and pattern of antibacterial use in specific area and compare with other centers. Subsequently, this information gives valuable perspective to develop local practice guidelines. Antibiotic administration local practice guidelines avoid unnecessary administration and improve therapeutic effectiveness. Another strategy is certain antibiotics or classes of antibiotics usage restriction. This method is applied to broad spectrums antibiotics (such as carbapenems), high risk for rapid antibiotic resistance (such as third-generation cephalosporins) and where toxicity is probable. Although there are lots of choices to reduce the inappropriate use of antibacterial, the most effective strategies will be multidisciplinary. Pharmacist cooperation, nursing staff, infection control, educated physicians, and infectious disease consultant are involved in multidisciplinary strategies. Policy makers should notice the concepts of population antibiotic consumption and give awareness to prescribers about their practices. All mentioned programs should also notice both on infection control development and engage rational antibiotic utilization in order to reducing future emergence of resistance strains and increasing overall antimicrobial efficacy. We should know that if we are not able to measure and compare our antibiotic consumption pattern, we will not reach to reasonable and effective antibiotics use.

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Conflict of interests

The authors claim that there is no conflict of interest.

References

1. Liem TY, Krediet TG, Fleer A, Egberts TC, Rademaker CM. Variation in antibiotic use in neonatal intensive care units in the Netherlands. *J Antimicrob Chemother.* 2010;65(6):1270-5. doi:10.1093/jac/dkq107
2. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. *JAMA.* 1995;274(8):639-44. doi:10.1001/jama.1995.03530080055041
3. Hanberger H, Garcia-Rodriguez JA, Gobernado M, Goossens H, Nilsson LE, Struelens MJ. Antibiotic susceptibility among aerobic Gram-negative Bacilli in intensive care units in 5 European countries. *JAMA.* 1999;281(1):67-71. doi:10.1001/jama.281.1.67
4. Goldmann DA, Weinstein RA, Wenzel RP,

- Tablan OC, Duma RJ, Gaynes RP, et al. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals. A challenge to hospital leadership. *JAMA*. 1996;275(3):234-40. doi:10.1001/jama.275.3.234
5. Kollef MH. Optimizing antibiotic therapy in the intensive care unit setting. *Crit Care*. 2001;5(4):189-95. doi:10.1186/cc1022
 6. Habibzadeh F. Use and misuse of antibiotics in the Middle East. *Lancet*. 2013;382:1175-82.
 7. Cars O, Molstad S, Melander A. Variation in antibiotic use in the European Union. *The Lancet*. 2001;357(9271):1851-3. doi:10.1016/S0140-6736(00)04972-2
 8. Kuster SP, Ruef C, Ledergerber B, Hintermann A, Deplazes C, Neuber L, et al. Quantitative antibiotic use in hospitals. Comparison of measurements, literature review, and recommendations for a standard of reporting. *Infection*. 2008;36(6):549-59. doi:10.1007/s15010-008-7462-z
 9. Hutchinson JM, Patrick DM, Marra F, Ng H, Bowie WR, Heule L, et al. Measurement of antibiotic consumption: A practical guide to the use of the Anatomical Therapeutic Chemical classification and Defined Daily Dose system methodology in Canada. *Can J Infect Dis*. 2004;15(1):29-35. doi:10.1155/2004/389092
 10. Goossens H, Ferech M, Vander Stichele R, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet*. 2005;365(9459):579-87. doi:10.1016/S0140-6736(05)17907-0
 11. Ansari F. Utilization review of systemic anti-infective agents in a teaching hospital in Tehran, Iran. *Eur J Clin Pharmacol*. 2001;57(6-7):541-6. doi:10.1007/s002280100350
 12. Salehifar E, Nasehi M, Eslami G, Sahraei S, Alizadeh Navaei R. Determination of Antibiotics Consumption in Buali-Sina Pediatric Hospital, Sari 2010-2011. *Iran J Pharm Res*. 2014;13(3):995-1001.
 13. Mousavi S, Behi M, Taghavi MR, Ahmadvand A, Ziaie S, Moradi M. Drug utilization evaluation of imipenem and intravenous ciprofloxacin in a teaching hospital. *Iran J Pharm Res*. 2013;12(Suppl):161-7.
 14. Monnet D, Mölstad S, Cars O. Defined daily doses of antimicrobials reflect antimicrobial prescriptions in ambulatory care. *J Antimicrob Chemother*. 2004;53(6):1109-11. doi:10.1093/jac/dkh230
 15. Ebrahimzadeh MA, Shokrzadeh M, Ramezani A. Utilization pattern of antibiotics in different wards of specialized Sari Emam University Hospital in Iran. *Pak J Biol Sci*. 2008;11(2):275-9. doi:10.3923/pjbs.2008.275.279
 16. Ansari F. Utilization review of systemic anti-infective agents in a teaching hospital in Tehran, Iran. *Eur J Clin Pharmacol*. 2001;57(6-7):541-6. doi:10.1007/s002280100350
 17. Pešić G, Jović Z, Vasić K. Application of the atc/DDD methodology to compare antibiotic utilization in two university hospital surgical departments. *Med Biol*. 2005;12(3):174-8.
 18. Kiiivet RA, Dahl ML, Llerena A, Maimets M, Wettermark B, Berecz R. Antibiotic use in 3 European university hospitals. *Scand J Infect Dis*. 1998;30(3):277-80.
 19. Guglielmo L, Leone R, Moretti U, Conforti A, Velo GP. Antimicrobial drug utilisation in hospitals in Italy and other European countries. *Infection*. 1994;22(S3):S176-81. doi:10.1007/bf01782703
 20. Johansen KS, Storgaard M, Carstensen N, Daschner F, Frank U. An international study on the occurrence of multi-resistant bacteria and aminoglycoside consumption patterns. *Infection*. 1988;16(5):313-22. doi:10.1007/bf01645084