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Research Article

Antibiotic utilization evaluation of inpatient and outpatient prescriptions in a rural general hospital in Iran

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ABSTRACT

Background: High rate of antibiotic prescription is commonly encountered in hospital settings. Although the problem of the irrational use of antibiotics is particularly acute in rural health centers of developing countries, antibiotic utilization studies in such areas are scarce. In this study, we aimed to compare antibiotic prescription patterns between inpatients and outpatients in a rural general hospital.
Methods: Inpatient and outpatient records were evaluated during a 1-month period. Data including patients' demographics, length of hospital stay, final diagnosis, antibiotic regimen, dosing, rout of administration, microbiological culture/sensitivity tests and other laboratory data were retrieved from the hospital information system.
Results: The number of prescriptions with at least one antibiotic was 686/1410 (48.6%) cases and 3812/6126 (62.2%) cases for inpatient and outpatient prescriptions, respectively. The mean number of antibiotic per prescription was 1.7±0.7 and 1.3±0.8 for inpatient and outpatients, respectively ($p<0.05$). Ceftriaxone had the highest rate of prescription among hospitalized patients with 791 (35.2%) times encounter while penicillin constituted the largest proportion of outpatient administrations with 2505 (29.8%) times. About 79% of inpatient and 62% of outpatient prescriptions containing final diagnosis data had the correct indication.
Conclusion: Our study showed that implementation of strict regulations for antibiotic use is extremely needed in this rural hospital. Establishing local guidelines, providing adequate education for healthcare professionals and putting restrictions for broad-spectrum antibiotic use can be beneficial.

Keywords: Drug utilization evaluation, Antibiotics, Rational prescription, Rural, Bacterial resistance

INTRODUCTION

Antibiotics are considered as one of the drug classes with a high prescription rate in hospital settings.[1] Studies show that about 33% of hospitalizations lead to antimicrobial therapy for patients.[2] High levels of antibiotic misuse such as inappropriate dosing or antibiotic prescription for viral infections have been documented in previous investigations.[3]

World Health Organization (WHO) conference of experts on the rational use of drugs held in Nairobi in 1985 suggested rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community.[4]

There are many factors contributing to the inappropriate use of antibiotics. Misdiagnoses due to human error, technical issues and factors related to pharmaceutical sales promotion are among the various reasons of antibiotic misuse.[2] The consequence of irrational and excessive use of antibiotics is deterioration of clinical and economic outcomes, which will subsequently lead to the emergence and spread of antibiotic-resistant species.[3] Eventually, antibiotic resistance can result in prolongation in hospitalization, failed treatments, raised healthcare costs and mortality rates.[2] The emergence of resistant bacteria both in humans and animals makes scrutinizing antibiotic utilization patterns more urgent since

this is a major determinant of outbreak and spread of these organisms.[5]

WHO defines drug utilization as the marketing, distribution, prescription and utilization of medications in society, with a special affirmation on the resulting medical, social, and economic outcomes.[6] Moreover, according to WHO definition, drug use evaluation (DUE) is a system of ongoing, systematic, criteria-based assessment of drug use that will help ensure that medicines are used in an appropriate manner at the individual patient level.[7] Medications with narrow therapeutic index, high price drugs as well as drugs, which their inappropriate use is accompanied by serious problems have been recommended as specific candidates for DUE studies.[8] DUE studies provide an opportunity to identify existing and possible drug-related problems that could prevent us from achieving optimum outcomes from pharmacotherapy, through their emphasis on the system of drug use.[4] Conducting DUE studies for antibiotics with a high prevalence of utilization, not only contributes to optimization of treatment but also has a positive impact on reducing treatment costs and the incidence of adverse drug events.[1]

In addition, DUE studies provide hospitals with valuable information to have an overview of their drug utilization patterns and take corrective measures and set guidelines to improve clinical practice. Many hospitals have attempted to tackle with the issue of antibiotic misuse by establishing guidelines and putting restrictions on the use of certain antibiotics aiming to reduce the phenomenon of bacterial resistance and prolong the life span of antibiotics.[4] It has also been reported that preparation of hospital formularies and organizing specialized committees in infections treatment may be beneficial in prevention of drug misuse.[9]

The problem of the irrational use of antibiotics is particularly acute in rural health centers of developing countries. In those countries, antibiotics are prescribed to 44-97% of patients in hospital and are often unnecessary.[10]

A recent study by James et al. which compared the antibiotic prescription patterns in urban and rural hospitals revealed that the antibiotic prescription was significantly higher in rural areas.[11] Therefore, studies on the antibiotic prescribing behavior of physicians and assessment of these prescriptions in developing countries are extremely needed. However, rational drug prescribing guidelines are implemented either insufficiently or ineffectively in many developing countries.[9]

The research on antibiotic use trends in rural areas especially in developing countries, where the phenomenon of antibiotic resistance seems to be more critical and requires more scrutinizing on physician's prescription behavior, is scarce. Despite the great importance of the subject, little research on antibiotic prescribing patterns has been conducted in rural areas of Iran.

In this study, we aimed to evaluate antibiotic prescribing patterns for inpatients and outpatients in a general hospital located in a rural area in Zanjan province, Iran.

METHODS

This study was a cross-sectional, retrospective, DUE study conducted in Amiral Momenin General Hospital. This 96-bed hospital is affiliated with Zanjan University of Medical Sciences, and it is the only hospital providing medical care in the rural region of Khodabandeh. The hospital includes medical, surgical, intensive care unit, gynecology and obstetrics, pediatric and neonatal wards as well as an emergency department.

Inpatients and outpatients who were prescribed at least one antibiotic from October 2014 to November 2014 were enrolled in this study. Data including patients' demographics, length of hospital stay, final diagnosis, antibiotic regimen, dosing, rout of administration, microbiological culture/sensitivity tests and other laboratory data were extracted from hospital information system (HIS) and for each patient one data collection form was filled. In cases that recorded information in HIS was incomplete or missing, data were extracted manually from the patient's file. The evaluation was performed for oral and parenteral antibiotics including antibacterial, antifungal and antiviral agents and we did not include topical antibiotics in our investigation. Patients who underwent dialysis were excluded from the study.

Study antibiotics were evaluated for their indication, dosing and duration of therapy based on diagnosis and microbiological culture according to information in two references of American Hospital Formulary Services and Applied Therapeutics.[12,13] We defined the appropriateness of prescription as concordance of physician's order with the administration information extracted from these two references. To avoid misinterpretation regarding the concordance of antibiotics indication with physician's diagnosis, we excluded the empiric therapies in the appropriateness evaluation for patients who had a microbial culture.

Possible drug-drug interactions between antibiotics and other medications were checked by two different references.[14,15] The percentage of prescriptions with one or more antibiotics and the number of antibiotics per prescription was determined. These measurements reflect antibiotic utilization from several different aspects. The proportion of prescriptions with at least one antibiotic is an indicator of the proportion of encounters that get antibiotics from the village hospital. The quantity of antibiotics per prescription demonstrates how many antibiotics were used at a time. The percentage of prescriptions with multiple antibiotics shows the extent of antibiotic combination therapy.

Statistical analysis of data was performed using SPSS software (version 16).

RESULTS

There were a total of 1410 inpatient and 6126 outpatient admissions during our study. The number of prescriptions with at least one antibiotic was 686 (48.6%) cases and 3812 (62.2%) cases for inpatient and outpatient prescriptions, respectively. Demographic data of the enrolled patients has been presented in Table 1. Twenty-six different types of antibiotics regardless of their route of administration were prescribed for hospitalized patients while there were 19 types of prescribed antibiotics for outpatients. Inpatient and outpatient antimicrobial encounter rate during the study period was 2243 times and 8403 times, respectively. Inpatient prescription included 1927 (85.9%) antibacterial, 301 (13.4%) antifungal and 15 (0.7%) antiviral agents while these figures for outpatients were 6945 (82.6%), 1268 (15.0%) and 190 (2.4%), respectively.

Cephalosporins, macrolides, and vancomycin were the classes of antibiotics that accounted for over 80% of inpatient prescriptions while penicillins, cephalosporins and macrolides constituted 80% of overall outpatient antibiotics.

Ceftriaxone had the highest rate of prescription among hospitalized patients with 791 (35.2%) times encounter while penicillin constituted the largest proportion of outpatient administrations with 2505 (29.8%) times.

Figures 1 and 2 illustrate the four highly prescribed antibiotics both for inpatients and outpatients.

The average number of antibiotic per total prescriptions was 1.7±0.7 and 1.3±0.8 for inpatient and outpatients, respectively ($p<0.05$).

The mean number of antibiotic in all antibiotic containing prescriptions was 2.8±1.5 for inpatients, which were significantly higher than the mean outpatient antibiotic encounter of all antibiotic containing prescriptions (1.9±1.2) ($p<0.05$).

Oral antibiotics constituted 24.9% of inpatient prescriptions and 52.9% of outpatient prescriptions. Parenteral antibiotics were used in 75.1% of inpatient and 47.1% of outpatient administrations.

Table 1: Demographic data of the patients.

Demographic data	Inpatients (%)	Outpatients (%)
Male	245 (35.7)	2194 (57.5)
Female	441 (64.3)	1618 (42.5)
Age±SD	28.3±22.7	25.2±19.3
Length of hospitalization (days)	4.6±3.8	-
0-6 age group	177 (25.8)	292 (7.7)
6-12 age group	55 (8.0)	1488 (39.0)
>12 age group	454 (66.2)	2032 (53.3)

SD: Standard deviation

Physician's final diagnosis, which resulted in antibiotic administration has been summarized in Table 2.

Regarding the antibiotic prescription patterns in different wards of the hospital, there were a total of 531 (23.6%) antibiotic prescription records for 217 patients in gynecology and obstetrics ward, 633 (28.3%) antibiotic records for 164 patients in internal ward, 88 (3.9%) records for 13 patients in ICU, 742 (33.1%) records for 222 patients in pediatric and neonatal ward and 249 (11.1%) records for 70 patients in surgical ward.

Appropriateness of antibiotic prescriptions was assessed for all prescriptions and for each ward separately.

Evaluation of appropriateness was not applicable for 2526 outpatient, and 64 inpatient antibiotic prescriptions since they lacked physician's diagnosis. For remaining

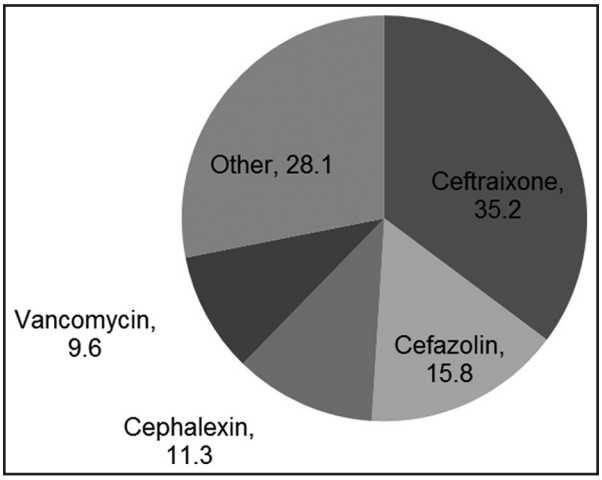

Figure 1: Four commonly prescribed antibiotics for inpatients.

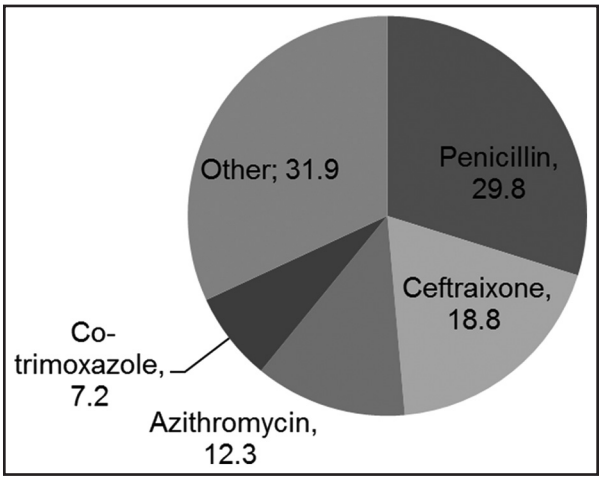

Figure 2: Four commonly prescribed antibiotics for outpatients.

prescriptions with a diagnosis, 1749 (61.8%) cases of antibiotic indications in outpatients matched with physician's diagnosis. The rate of indication appropriateness for inpatients was 1637/2070 (79.0%).

Of 2829 assessable outpatient prescriptions, 1708 (60.4%) cases were in concordance with our study references in terms of prescribed dose. However, in 718 (25.4%) cases patients received excessive dose and in 403 (14.2%) cases the prescribed dose was sub-therapeutic.

Assessment of inpatient dosing patterns showed that the prescribed dose was acceptable according to our study references in 1526 (73.7%) records. Ordered dose was either sub-therapeutic or excessive in 368 (17.8) and 176 (8.5%) cases, respectively.

Regarding the duration of treatment, 1501 (53.0%) records of outpatient antibiotics found to be appropriate. In 929 (32.9%) records patients received antibiotics for a shorter course of time than the appropriate duration of treatment while 399 patients (14.1%) received antibiotics for a longer time than it was appropriate for their indication.

For hospitalized patients, on the other hand, appropriate duration of treatment was encountered in 1371 (66.2%) cases, while in 500 (24.2%) records the duration of treatment tended to be shorter and in 199 (9.6%) cases patients were administered antibiotics for a longer duration of time.

Table 2: Final diagnosis of physicians leading to antimicrobial prescription.

Diagnosis	Inpatients (%)	Outpatients (%)
Pneumonia and respiratory infections	162 (23.6)	602 (15.8)
Gastrointestinal infections	54 (7.9)	319 (8.4)
Sepsis	68 (9.9)	-
Pyelonephritis and urinary tract infections	52 (7.6)	213 (5.6)
Soft tissue and skin infections	22 (3.2)	152 (4.0)
Fever and convulsion	37 (5.4)	-
Drug poisoning	2 (0.3)	-
Surgical prophylaxis	225 (32.8)	-
No diagnosis	64 (9.3)	2526 (66.2)
Total	686 (100)	3812 (100)

According to our findings, microbial cultures and antibiotic sensitivity tests were ordered by physicians for 285 (41.5%) antibiotic - receiving hospitalized patients while tests were performed in only 45 (1.2%) cases of outpatients.

For hospitalized patients with a microbial culture and a sensitivity test, the rate of indication appropriateness was 90.7%. Moreover, the rate of indication appropriateness for outpatients with a culture was 77.7%.

Additionally, we compared the appropriateness of antibiotic prescription among different wards of the hospital. Table 3 demonstrates the results of this evaluation.

Major drug-drug interactions between antibiotics and other concomitantly prescribed medications for inpatients were observed in 38 (1.7%) records. Of these serious interactions, 28 interactions were due to concomitant use of antibiotics with anticoagulant agents (e.g. heparin and enoxaparin). The incidence of serious drug-drug interaction was 1.1% (99 records) among outpatients.

We could not find a positive correlation between the variables of hospitalization days and the amount of antibiotics received by a patient (correlation coefficient (r)=0.31).

Broad-spectrum antibiotics' utilization pattern was evaluated in all included wards. Three main broad-spectrum antibiotics, including cefepime, piperacillin/tazobactam and ampicillin/sulbactam were prescribed 58 times during the 4 weeks study period. Internal ward and ICU were the two wards with 39 (67.2%) and 19 (32.8%) broad-spectrum antibiotic record. For 49 patients who were prescribed a broad-spectrum antibiotic, antibiotic sensitivity test was conducted in 20 (40.8%) patients.

DISCUSSION

Our study results showed a higher percentage of antibiotic prescription among outpatients compared to hospitalized patients (62.2% vs. 48.6%). These figures are comparable with antibiotic prescription rates in other developing countries like

Table 3: Comparison of antibiotic prescription appropriateness in different wards.

Ward	Number of antibiotic prescriptions	Appropriate indication (%)	Appropriate dose (%)	Appropriate duration (%)
Internal	633	409 (64.6)	350 (55.2)	322 (50.8)
Gynecology and obstetrics	531	408 (76.8)	371 (69.8)	372 (70.0)
Pediatric and neonatal	742	586 (78.9)	591 (79.6)	488 (65.7)
ICU	88	62 (70.4)	62 (70.4)	60 (68.1)
Surgical	249	172 (69.0)	152 (61.0)	129 (51.8)
Total	2243	1637 (72.9)	1526 (68.0)	1371 (61.1)

ICU: Intensive care unit

Yemen where approximately 50% of prescriptions contain an antibiotic.[16] Another study conducted in the rural areas of a developing country showed the same trend in higher prevalence of antibiotic encounter among outpatients.[17]

Despite the lower percentage of inpatients with at least one antibiotic encounter, the average number of antibiotics for inpatients was significantly higher than outpatients ($p<0.05$). The average number of antibiotics in a prescription is considered a valuable indicator of prescription rationality. Physicians are expected to keep this mean at the lowest level possible to prevent multi-drug interactions and the emergence of bacterial resistance.[18] Serious medical conditions in hospitalized patients as well as the probability of acquiring nosocomial infections may lead to an elevated number of antibiotics in prescriptions. Nevertheless, this high rate conflicts with the notion that antibiotic use is expected to be more rational in hospital setting than the community since there is more vigilance on patients' pharmacotherapy.

Compared to antibiotic utilization rates in a developed country like the United States where the average number of antibiotic per prescription was found to be 0.88±0.15 in outpatients[19] the average number of 1.7±0.7 for inpatients and 1.3±0.8 for outpatients seems to be a great concerning issue.

In a previous antibiotic utilization study in Tehran, the capital city of Iran, the approximate number of antibiotic per prescription was 1.2 antibiotic per prescription. The average number of antibiotics for either of inpatients and outpatients was higher in our study. Similar results have been derived from a research in Netherlands which found that antibiotic use prevalence was significantly higher in rural areas.[20]

Two main diagnoses for inpatients leading to antibiotic therapy were surgical prophylaxis followed by respiratory infections. The rate of c-section procedures is considerably high in this center leading to increased rate of surgical prophylaxis. Respiratory infections and gastroenteritis were diagnosed for most of the outpatients.

The rate of appropriate indication for antibiotics in the outpatient group was 61.8% compared to 72.0% appropriateness in inpatient group. A previous study by Evirgen et al. found a 59.7% of proper antibiotic use among hospitalized patients.[21] In spite of mentioned indication appropriateness figures, the antibiotic indication matched with our study references in 90.7% of inpatients and 77.7% of outpatients whom were ordered a microbial culture and antibiotic sensitivity test. This can be an indicator of the great importance of conducting these tests to improve decision making on antimicrobial treatment.

Pediatric and neonatal ward had the highest rate of indication and dosing appropriateness among wards. This can be a result of pediatric specialists' competent knowledge and training, performing regular microbial cultures along with close monitoring of patients in this ward.

Inappropriate dosing which we mainly encountered in internal ward may be a result of failing to tailor pharmacotherapy for each individual. The main cause leading to dose errors was overlooking patients' renal function and the lack of drug dose adjustment based on creatinine clearance.

Shorter duration of treatment was frequently encountered in this investigation. This may be due to insufficient capacity of this hospital in spite of its great load of daily patient visits. Consequently, discharge of hospitalized patients could have happened earlier than the optimum time. Since we did not follow-up discharged patients, we were not able to assess the continuation of their antimicrobial therapy.

A recent study by Battleman et al. showed that appropriate antibiotic selection is significantly associated with shorter length of hospital stay.[22] We tried to find any positive correlation between the quantity of prescribed antibiotics with the length of hospitalization, however, we could not find a possible correlation between these two factors (correlation coefficient (r)=0.31).

Although the presence of physician's final diagnosis is an essential component of a patient's record, two-third of the evaluated outpatient records were lacking diagnosis. This limitation of our study led to an incomplete appropriateness assessment for outpatients since we were not able to check if the indication matched the existing diagnosis.

CONCLUSION

High ratio of antibiotic prescription in our hospital necessitates taking a prompt corrective action. To achieve a better and rational antibiotic consumption, we ought to promote the use of microbiological data and provide education for healthcare professionals. Also, implementation of strict regulations is extremely needed in this rural hospital. Establishing local guidelines and putting restrictions for broad-spectrum antibiotic use can be beneficial.

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