RESEARCH ARTICLE

PATTERN OF ANTIMICROBIAL PRESCRIBING AMONG IN-PATIENTS OF A TEACHING HOSPITAL IN YEMEN: A PROSPECTIVE STUDY

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ABSTRACT

Objectives: The irrational use of antimicrobials leads to a number of consequences in terms of cost, drug interactions, hospital stay and bacterial resistance, and a substantial economic burden on health care systems. This study aimed to investigate the pattern of antimicrobial use among hospitalized patients.

Methods: The treatment-charts for 384 in-patients admitted to the major wards (medicine, surgery, pediatric and gynecology) in the teaching hospital and receiving antimicrobials were reviewed for the period from February to May 2016. The enrolled patients were observed from admission till discharge. Descriptive statistics were applied to the collected data and institutional ethical committee approval was obtained prior to the study. The majority of patients were females (52.86%), their age from 1 to 16 years (59.63%).

Results: The common diagnosis for patients was respiratory tract infections (30.21%) followed by gastrointestinal infections (19.53%). Ceftriaxone (50.52%) was the top most frequently used antimicrobials followed by ampicillin (37.50%), cefotaxime (16.15%), cefuroxime (15.89%), metronidazole (11.72%) and amoxicillin/clavulanic acid (5.99%). The majority of the admitted patients (63.54%) received two or more antimicrobials. 45.4% of physicians confirmed the influence of drug companies and their drug promotion on their antimicrobial prescribing.

Conclusion: The evidence of high prescribing rate of ceftriaxone in the presence of other antimicrobials, low-price and suitable antimicrobials reflected irrational prescribing and this may be responsible on developing resistance against ceftriaxone and other cephalosporins.

Keywords: antimicrobials, ceftriaxone, prescribing, Yemen.

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INTRODUCTION

Rational use of drugs is based on use of right drug, right dosage at right cost which is well reflected in the world health organization (WHO) definition: "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, at the lowest cost to them and their community". Appropriate drug utilization has a huge contribution to global reduction in morbidity and mortality with its consequent medical, social and economic benefits. Inappropriate prescribing is known all over the world as a major problem of health care delivery. This is more so in developing countries where health budgets are small and 30-40% of the total health budget is spent on drugs. Antimicrobials are one of the most common groups of drugs prescribed in hospitals. It has been estimated that up to third of all patients received at least one antibiotic during hospitalization. AMs along with vaccines and oral rehydration salts represent potential agents in preventing mortality as well as morbidity. Widespread usage of antibiotics in hospitals has also been associated with increases in bacterial strains and species that no longer respond to treatment with the most common antibiotics. Common forms of antibiotic misuse include excessive use of prophylactic antibiotics in travelers, failure of medical professionals to prescribe the correct dosage on the basis of the patient's weight and history of prior use, failure to take the entire prescribed course of the antibiotic and incorrect administration. Immethodical use of antibiotics has become a serious problem and even the world could finally return to the pre antibiotic era. Over prescribing of antibiotics, not only increases the costs of health care, but may result in super infection due to resistant bacteria, as well as opportunistic fungi, and may increase the likelihood of an adverse drug
reaction\(^{13}\). It is impossible to introduce correct and rational use of antimicrobials without identification of current situation in their consumption\(^{14}\). Therefore, periodic assessment of the prescribing practices in health facilities will help to identify specific drug use problems and provide policy makers with relevant information that could be useful in review of policies of drug procurement and drug prescribing practices in the affected institutions and regions\(^2\). This study aimed to evaluate the prescribing pattern of antimicrobials among hospitalized patients and also find out the factors that influence prescribing practice.

**SUBJECTS AND METHODS**

This was a prospective descriptive study conducted in the teaching hospital after obtaining approval from the institutional ethical committee of faculty of medicine at Thamar region, Yemen (TUMEC-16052). The treatment charts of 384 inpatients were reviewed during the period of four months (February to May 2016). The wards of the hospital were visited daily by the research assistants and/or the researcher\(^8\).

**Inclusion criteria**

All admitted patients in the major wards (medicine, surgery, pediatric and gynecology) in the teaching hospital and receiving antimicrobial therapy.

**Exclusion criteria**

- The out-patients
- Patients who admitted to intensive care units.
- Patients who are not receiving antimicrobials.
- Pregnant and nursing mothers.

A standard Performa was designed for collecting patient details such as name, age, gender, and diagnosis, date of admission and date of discharge in addition to the specific issues related to antimicrobial use as name of antimicrobials, dosage schedule and route of administration\(^2\). A questionnaire related to the factors that contribute to prescribing practices were distributed to 33 clinicians who work in the teaching hospital. The identified ten factors were patient’s factors (demand and socio-economic status), prescriber’s factors (diagnosis, culture media lab report, in-service education, workload and feedback from patient), drug factors (availability and cost) and influence of industry (drug promotion)\(^6\). After necessary processing, all data were entered into the computer and using Statistical Package for the Social Sciences (SPSS), Version 20 for analysis. Chi square test was used to test the association between group variables. The level of significance was accepted at P value < 0.05.

**RESULTS**

A total of 384 admitted patients’ treatment-charts were reviewed. The majority of patients were females (52.86%) and most of them were from 1 to 16 years (59.63%). The highest number of patients was admitted to pediatric ward (60.15%), followed by equal number from surgery and medicine wards (16.93% and 16.15% respectively) (Table 1). Parenteral intravenous injections remain relatively common route of administration (99.7%) of the reviewed patients chart.

| Variables               | Number of patients (n=384) | Percentage (%) |
|-------------------------|---------------------------|----------------|
| **Sex**                 |                           |                |
| Male                    | 181                       | 47.14%         |
| Female                  | 203                       | 52.86%         |
| **Age**                 |                           |                |
| 1-16                    | 229                       | 59.63%         |
| 17-60                   | 132                       | 34.38%         |
| > 60                    | 23                        | 5.99%          |
| **Medical ward**        |                           |                |
| Internal medicine       | 62                        | 16.15%         |
| Surgery                 | 65                        | 16.93%         |
| Pediatric               | 231                       | 60.15%         |
| Gynecology              | 26                        | 6.77%          |

The most general diagnosis for patients was respiratory tract infections (30.21%), followed by gastrointestinal (19.53%) and neurological diseases (13.02%). Fractures and traumas were at the end of the order with 1.04% of the total diagnosis (Table 2).

| General diagnosis        | No. of patients (n=384) | Percentage (%) |
|-------------------------|-------------------------|----------------|
| Neurological diseases    | 50                      | 13.02%         |
| Cardiovascular diseases  | 9                       | 2.34%          |
| Respiratory diseases     | 116                     | 30.21%         |
| Renal diseases           | 10                      | 2.60%          |
| Gastrointestinal diseases| 75                      | 19.53%         |
| Metabolic diseases       | 10                      | 2.60%          |
| Hematologic diseases     | 6                       | 1.56%          |
| Endocrine diseases       | 23                      | 5.99%          |
| Infectious diseases      | 11                      | 2.86%          |
| Surgical states          | 42                      | 10.93%         |
| Fractures & traumas      | 4                       | 1.04%          |
| Others                   | 28                      | 7.29%          |

Moreover, the results revealed the great diversity of antimicrobials used for the treatment of the hospitalized patients. In this study, the top frequently used antimicrobial was ceftriaxone (50.52%) followed by ampicillin (37.50%), cefotaxime (16.15%), cefuroxime (15.89%), metronidazole (11.72%), and amoxicillin/clavulanic acid (5.99%) (Table 3). Hospital’s physicians preferred to prescribe antimicrobials in combination for the treatment of the admitted patients. The majority of them (63.54%) received two or more antimicrobials (55.73% of them received two antimicrobials and 7.81% received three antimicrobials), while the rest of the patients (36.46%) received single antimicrobial (Table 4).

Regarding the physician questionnaire about the factors that affect prescribing of antimicrobials, the results showed that most contributing factor is the clinical diagnosis (100%), followed by the other factors as culture media lab report, availability and cost of drugs (87.9%). 45.4% of physicians agreed on the influence of drug companies and their drug promotion on the antimicrobial prescribing (Table 5).
DISCUSSION

The discovery of antibiotics is considered as one of the important medical achievements in the 20th century. Antibiotics had a tremendous impact on improving the life quality of human and represent one of the most commonly used drugs\(^1\). Antibiotic resistance has been directly linked to high levels of antibiotic consumption within the community\(^2\). About 30-50% of hospitalized patients receive at least one antibiotic for therapy or prophylaxis during their hospitalization. Also, there is evidence that antibiotics usage in hospitals is increasing, and that over a third of prescriptions are not compliant with evidence-based guidelines\(^3,5,9,10,11,13\). Several factors have appeared to be the reasons for irrational prescribing patterns such as the use of drugs that are not linked to the diagnosis, inappropriate dose and duration of therapy\(^6,14\) in addition to the self-medication by individual patients regardless of the causing pathogen\(^7\). This irrational use of antimicrobials leads to a number of consequences in term of cost, adverse drug interactions, hospital stay and bacterial resistance, and a substantial economic burden on health care systems\(^8\).

A study of prescribing patterns of antimicrobials is an effective way of reflecting appropriateness use. A prescription provides an insight into a prescriber’s attitude to the disease being treated and the nature of health care delivery system in a community and/or a country\(^1,3,5,18\). There are many studies related to antibiotic use in hospitals. The resulted data provide a constructive approach in solving problems arising from multiple antibiotic use\(^19,20\). This study was done on the 384 hospitalized

| Antimicrobials | Medicine No. | Surgery No. | Paediatric No. | Gynaecology No. | Total (n=658) No. | % |
|---------------|--------------|-------------|----------------|-----------------|------------------|---|
| Amikacin      | -            | 4           | 5              | -               | 9                | 1.37 |
| Amoxicillin   | 2            | -           | 1              | -               | 3                | 0.46 |
| Amoxicillin /Clavulanic Acid | 7 | 10 | 5 | 1 | 23 | 3.50 |
| Ampicillin    | 5            | 2           | 125            | 12              | 144              | 21.88 |
| Ampicillin/Subactam | - | - | 14 | - | 14 | 2.13 |
| Ampiclox      | -            | -           | 17             | 1               | 18               | 2.74 |
| Azithromycin  | -            | -           | 4              | -               | 4                | 0.61 |
| Cefepime      | 1            | 3           | 2              | -               | 6                | 0.91 |
| Cefixime      | -            | 1           | 1              | -               | 1                | 0.15 |
| Cefotaxime    | 5            | 2           | 55             | -               | 62               | 9.42 |
| Ceftriaxone   | 32           | 40          | 105            | 17              | 194              | 29.50 |
| Cefuroxime    | 11           | 10          | 40             | -               | 61               | 9.27 |
| Ciprofloxacin | 2            | 1           | -              | -               | 3                | 0.46 |
| Clarithromycin| 4            | -           | 5              | -               | 9                | 1.37 |
| Co-Trimoxazole| 1            | 1           | 3              | -               | 5                | 0.76 |
| Erythromycin  | 1            | 6           | -              | -               | 7                | 1.06 |
| Gentamicin    | -            | 2           | 13             | -               | 15               | 2.28 |
| Kanamycin     | -            | 1           | 4              | -               | 5                | 0.76 |
| Levofloxacin  | 2            | 1           | 1              | -               | 4                | 0.61 |
| Metronidazole | 6            | 18          | 21             | -               | 45               | 6.84 |
| Moxifloxacin  | 2            | -           | -              | -               | 2                | 0.30 |
| Ofloxacin     | -            | 1           | -              | -               | 1                | 0.15 |
| Penicillin G  | 3            | -           | -              | -               | 3                | 0.46 |
| Rifampicin    | 1            | -           | -              | -               | 1                | 0.15 |
| Rosifloxacin  | -            | -           | 2              | -               | 2                | 0.30 |
| Vancomycin    | 3            | -           | 13             | -               | 16               | 2.43 |
| Ceftazidime   | 1            | -           | -              | -               | 1                | 0.15 |

**Figure 1:** Prescribed antimicrobial agents
patients who admitted internal medicine, pediatric, surgery and genecology departments in the teaching hospital in Thamar, Yemen, from February to May 2016. The age distribution of patients showed that the age group from 1 to 16 years constituted 59.63% of the study population. No much variation between males (47.14%) and females (52.86%) was noted.

Table 4: Antimicrobials according to the combination with others.

| No. of prescribed antimicrobials (AMs) | No. of patients (n=384) | Percentage (%) |
|---------------------------------------|-------------------------|----------------|
| Single AMs                            | 140                     | 36.46          |
| Combination of two AMs                 | 214                     | 55.73          |
| Combination of three AMs               | 30                      | 7.81           |

These results are not compatible to the study conducted by Rosman et al., in France and Netherlands where the mean age of study population was 50.5±7.7 years. The high percentage of antimicrobials administered by intravenous route (99.7%) was consistent with other findings in which the injections were most common route of antibiotic administration in hospitalized patients. Also, it might be explained that doctors being under pressure to prescribe rapid-acting drugs to get fast improvement especially in acute infections.

Regarding the type of infections, our results were compatible with other studies that classified the upper respiratory tract diseases as the most common infection. Moreover, recent estimates indicate that 1.9 million children worldwide die each year from acute respiratory illnesses, many of which are lower respiratory infections as pneumonia.

Table 5: Factors influence prescribing of antimicrobials.

| Factor                              | No. (n=33) | % |
|-------------------------------------|------------|---|
| Clinical diagnosis                  | 33         | 100          |
| Culture report                      | 29         | 87.9         |
| Feedback from patient responses     | 28         | 84.85        |
| Influence of drug companies         | 15         | 45.4         |
| (Medical representatives)           |            |              |
| Availability of drugs               | 29         | 87.9         |
| Cost of drugs                       | 29         | 87.9         |
| Patient’s demand                    | 28         | 84.8         |
| In-service education                | 16         | 48.5         |
| Socio-economic status of patient    | 28         | 84.9         |
| Clinician’s workload                | 21         | 63.7         |

Ceftriaxone was the most frequently used antimicrobials (50.52%) followed by ampicillin (37.50%), cefotaxime (16.15%), cefuroxime (15.89%) and metronidazole (11.72%). The studies conducted in China and India were confirmed our findings and illustrated that cephalosporins were the most prescribed. Conversely, this ranking was not consistent with the pattern of antimicrobial use observed in other studies which found that macrolides were the most prescribed class of antibiotics.

In addition, Kumar et al., found that metronidazole is the most prescribed. The high prescribing of cephaporsins in this study could be attributed to their broad spectrum of activity against most gram-positive and gram-negative bacteria, including several strains resistant to other antibiotics, and recommended for serious infections caused by susceptible microorganisms. Metronidazole also prescribed in higher rate because it is the drug of choice in the treatment of anaerobic bacterial infections. Although, ceftriaxone with fluoroquinolones and macrolides consider the preferred antimicrobials for respiratory tract infections that were the most diagnosis in the current study, this high prescribing rate of ceftriaxone reflected irrational prescribing of antimicrobials and it may be responsible on developing bacterial resistance. Moreover, there are many contributing factors for this irrational prescribing such as the wide available trade names of ceftriaxone in Yemeni market that leads to competition between pharmaceutical companies to distribute them, in addition to increasing the temptations to physicians to prescribing ceftriaxone. The majority of the admitted patients received two or more antimicrobials in different combinations (63.54%). This prescribing is a practice commonly observed in Yemen as well as in other regions. These findings are agreed with the study conducted in Nepal and other countries and also with the WHO guidelines. The predominant use of a combination of antimicrobials may be due to the fact that physicians try to expand the possible spectrum of action to include all expected microbes by prescribing combination of antimicrobials. The other reasons to such practices were probably the availability of drugs, its costs and the culture media lab report. On the other hand, these combinations have every possibility of producing more adverse reaction(s) and/or changing microbial ecology in addition to the increased costs of the therapy to the patients concerned as well as to the health care system. Antonio da Cunha et al., in Brazil showed that 28% of the antibiotic prescriptions for children with acute respiratory infection were inappropriate. Finally, the results showed that most contributing factor that influences the prescribing is the clinical diagnosis (100%), followed by all of culture media Lab report, availability and cost of drugs (87.9%). These results are not consistent with the study occurred in Malaysia, which showed that drug availability (97.1%) and cost of drug (88.6%) are the most factors influencing the prescription of antimicrobials. Moreover, 45.4% of physicians agreed on the influence of drug companies and their drug promotion on the antimicrobial prescribing. Actually, this is a mutual factor on prescribing of other drugs because most of drug companies entice doctors to prescribe their products regardless the patient-need and the international therapeutic guidelines.

CONCLUSION

There is irrational and inappropriate use of antimicrobials. This practice may be leads to a number of consequences in term of cost, adverse drug interactions, bacterial resistance and a substantial economic burden on health care systems.
diagnosis, culture media lab report and availability and cost of drugs are major factors influencing prescribing, although, the selection of antimicrobials may be the personal choice/preference for some physicians. Additional studies on large scale in different health sectors are required to further explore patterns of antimicrobial prescribing and to improve perceptions and attitudes of physicians to play more active role in rational prescribing and to reduce the development of resistance.

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AUTHOR’S CONTRIBUTION
The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST
No conflict of interest associated with this work.

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