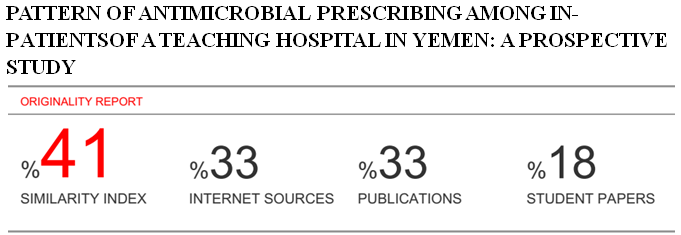
**Reviewer’s Comments**

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

## **Abstract:**

## Antimicrobials represent one of the most commonly used drugs. Their irrational use leads to a number of consequences in term 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 hospitalizedpatients in different medical wards. A total of 384 admitted patients' treatment-charts were reviewed for antimicrobial prescribing. The majority of them were females (52.86%), most of the patients were from 1 to 16 years (59.63%) and intravenous injections remain relatively the common route of administration (99.7%). Most of patients were diagnosed as respiratory tract infections (30.21%) followed by gastrointestinalinfections (19.53%), fractures & traumas were at the end of the order with 1.04% of the total diagnosis. Ceftriaxone (50.52%) wasthe 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 in different combinations for their treatments while only 36.46% of patients treated by single antimicrobial drug. All the physicians agreed that clinical diagnosis is the important factor fordetermination of prescribed antimicrobials(100%), followed by other factors such as culture report, availability and cost of drugs (87.9%). 45.4% of physicians confirmed the influence of drug companies and their drug promotion on their antimicrobial prescribing.

## **Key words: antimicrobials, prescribing, ceftriaxone, Yemen.**

## **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" 1,2.

Appropriate drug utilization has a huge contribution to global reduction in morbidity and mortality with its consequent medical, social and economic benefits 3,4. 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 3,5,6.

Antimicrobials are one of the most common groups of drugs prescribed in hospitals7,8. 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 9.

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 antibiotics10. 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 administration11.

Immethodical use of antibiotics has become a serious problem and even the world could finally return to the pre antibiotic era 12. Over prescribing of antibiotics, not only increases the costs of health care, but may result in superinfection 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 problemsand 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 regions2. Thisstudy aimed to evaluate the prescribing pattern of antimicrobials among hospitalized patients in medical wards and also find out the factors that influence prescribing in order to promote the rational use of antimicrobials.

**Methodology:**

This was a prospective descriptive study during the period of three months (February to April 2016) after obtaining approval from the institutional ethical committee of the teaching hospital at Thamar region, Yemen.

The treatmentcharts of 384 admitted patients who were receiving antimicrobial therapy in the medicalwards of internal medicine, surgery, pediatric and gynecology departments were reviewed. The ICU patients, pregnant women and nursing mothers were excluded in this

study.The wards of thehospital were visited daily by the research assistants and/or the researcher.

A standard performa was designed for collecting patient details such as name, age, gender, date of admission, clinical diagnosis and specific issues related to antimicrobial usesuch as name of antimicrobials, their dosage schedule, route of administration and date ofdiscontinuation. Each patient was followed on a daily basis untilhis/her discharge from the hospital.Furthermore, aquestionnaire formwasdistributed for physiciansregardingthe most important factors that influence prescribing of antimicrobials in the hospital.

After necessary processing, all data were entered intothe computer-based statistical programme - Statistical Package for the Social Sciences(SPSS), Version 20 for Windows for analysis. The processed data were analyzedaccordingly.

**Results:**

A total of 384 admitted patients' treatment-charts were reviewed. The majority of them were females (52.86%). Most of the patients were from 1 to 16 years (59.63%), followed by patients with age from 17 to 60 years (34.38%). The highest number of the admitted patients was from pediatric ward (60.15%), followed by equal number from surgery and medicine departments (16.93% and 16.15% respectively).**(Table 1)**

Parenteral intravenous injections remain relatively common route of administration (99.7%) of the reviewed patients chart**.**The most general diagnosis for patients was upper respiratory tract infections (30.21%), Followed by gastrointestinal (19.53%) and neurological diseases (13.02%). Fractures & traumas were at the end of the ranking with 1.04% of the total diagnosis.**(Table 2)**

Moreover, the results revealed the great diversity antimicrobials used for the treatment of the admitted patients among medical wards. In this study, the top most 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%).**(Figure 1;Table 3)**

Hospital`s physicians preferred to prescribe antimicrobials in combination for the treatment of the admitted patients. The majority of the admitted patients (63.54%) received two or more antimicrobials, 55.73% of them received two antimicrobials and 7.81% received three antimicrobials in combination, 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 all of culture report, availability of drugs 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. Antibiotics had a tremendous impact on improving the life quality of human and represent one of the most commonly used drugs15.

Antibiotic resistance has been directly linked to high levels of antibiotic consumption within the community 16. 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 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 therapy6,14 in addition to the self-medication by individual patients regardless of the causing pathogen 17.Thisirrational 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 systems7.

A study of prescribing patterns of antimicrobials is an effective way of reflecting appropriateness of antimicrobial 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 country1,3,5,18.

There are many studies related to antibiotic usein hospitals. The resulted data provide aconstructive approach in solving problems arising frommultiple antibiotic use19,20.This study was done on the 384hospitalized patients who admitted internal medicine, pediatric, surgery and genecology departments in the teaching hospital in Thamar, Yemen, from Febrauary to April 2016.

The age distribution of patients showed that the age group from 1 to 16 years constituted 59.63% of the study population.No muchvariation between males (47.14%) and females (52.86%) wasnoted in the study population. These results are not compatible to the study conducted by Rosman*et al*., 2007 in France andNetherlands where the mean age of study population was50.5±7.7 years21.

The high percentage of antimicrobials administered by intravenous route (99.7%)was consistent with other findings in which the injectionsare 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 infections6,7.

Regarding the type of infections, our results were compatible with other studies that classified the upper respiratory tract diseases as the most common infection20. 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 22.

Ceftriaxone was the most frequently used antimicrobials (50.52%) followed by ampicillin (37.50%), cefotaxime (16.15%), cefuroxime (15.89%) andmetronidazole (11.72%).The studies conducted in China and India were confirmed our findings and illustrated thatcephalosporins were the most prescribed5,20,23.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 antibiotics24,25.In addition, Vivekkumar*et al*. found that metronidazole is the most prescribed 4.

The highestprescribing of cephalosporins 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 microorganisms6,26. Metronidazole also prescribed in higher rate because it is the drug of choice in the treatment of anaerobic bacterial infections 26.

Although, ceftriaxone withfluoroquinolones and macrolides consider the preferred antimicrobials for respiratory tract infections - that were the most diagnostic diseases in the current study-, this high prescribing rate of ceftriaxone in the presence of other available, low-price andsuitable antimicrobials reflect irrational prescribing of drugs and this may be responsible on developing resistancefrom microbes against ceftriaxone and other cephalosporins. There aremany contributing factors for this irrational prescribing such as the wide available trade names of ceftriaxone in Yemeni market and thisleads to competition between pharmaceutical companies to distribute them, in addition to increasing the temptations to physicians to prescribing ceftriaxone20,26.

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 regions6,20,21,27. These findings are agreed with the study conducted in Nepal and other countries and also with the WHO guidelines 6,7,28.

The predominant use of a combination of antimicrobials may be due to the fact that physicians try to expand the possible spectrum of action of antimicrobials to include all expected microbes by prescribing combination with different mechanism of action and activity.The other reasons to such practices were probably the availability of drugs, its costs and the culture report6,20.

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 8. Antonio da Cunha et al in Brazil showed that 28% of the antibiotic prescriptions for children with acute respiratory infection were inappropriate 27.

Finally,the results showed that most contributing factor that influences the prescribing is the clinical diagnosis (100%), followed by all of culture 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 6. 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 all drugs and every company entices doctors to prescribe their products regardless the patient-need and the international therapeutic guidelines1,28,29.

**Conclusion:**

On the light of the current results, it could be concluded thatthere is a polypharmacy, irrational,overuse and inappropriate use of antimicrobials. Ceftriaxoneespecially and cephalosporinsgenerallywere the most commonly prescribed antimicrobials.Clinical diagnosis, culture 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 encourage periodic assessment of the sensitivity pattern of pathogenic organisms to avoid antimicrobial resistance. Also,there is an urgent need to develop strict policy for prescribing antimicrobials to improve perceptions and attitudes of physicians to play more active role in rational prescribingand to reduce the development of resistance.

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**Conflict of interest:**

No conflict of interest associated with this work.

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**Tables and Figures:**

**Table 1: Demographic profile for patients.**

|  |  |  |
| --- | --- | --- |
| **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% |

**Table 2: Distribution of patients based on the general diagnosis.**

|  |  |  |
| --- | --- | --- |
| **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% |

**Figure 1: Prescribed antimicrobial agents.**

**Table 3: Distribution of antimicrobials according to medical wards.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Antimicrobials** | **Medical wards** | | | | **Total (n=658)** | |
| **Medicine** | **Surgery** | **Pediatric** | **Gynecology** |
| **No.** | **No.** | **No.** | **No.** | **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/Sulbactam | - | - | 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 | 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% |

**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% |

**Table 5: Factors influence prescribing of antimicrobials.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Factor** |  | |
| **No.** | **% (n=33)** |
| 1 | Clinical diagnosis | 33 | 100% |
| 2 | Culture report | 29 | 87.9% |
| 3 | Feedback from patient responses | 28 | 84.85% |
| 4 | Influence of drug companies  (Medical representatives) | 15 | 45.4% |
| 5 | Availability of drugs | 29 | 87.9% |
| 6 | Cost of drugs | 29 | 87.9% |
| 7 | Patient's demand | 28 | 84.8% |
| 8 | In-service education | 16 | 48.5% |
| 9 | Socio-economic status of patient | 28 | 84.9% |
| 10 | Clinician's workload | 21 | 63.7% |