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Research Article

Appropriateness of Antimicrobial Therapy and Pattern of Antimicrobial Resistance in the Teaching Hospital

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Abstract:

Irrational antibiotic therapy contributes to developing antibiotic resistance, which is a worldwide problem of significant mortality, morbidity and increased health-care costs. For prevention of antibiotic resistance, it is necessary to stop irrational antibiotic therapy through increasing awareness among physicians and to provide a base for formulating rational antibacterial guidelines. To achieve this goal, an audit was done to assess the inpatient rational usage pattern of antibiotics in a teaching hospital and, as such, study is not yet done in Bangladesh. The cross-sectional observational study was done on admitted patients of the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder (BIRDEM) General Hospital of the capital city of Bangladesh who were treated with antibiotics prescribed to the majority of undiagnosed 63.1% patients. Gastrointestinal (18.03%), gynecological and obstetrical (16.39%), urogenital (14.20%) and dermatological disease (11.20%) were the important entity of studied patients. At admission, antibiotics were empirically prescribed to 48.80% of patients. More patients were treated with single antibiotics (61%) by the oral (5.4%) and parenteral (94.6%) route. The highest resistance was reported to pipercillin (81.8%) while the lowest resistance was to amikacin (63.6%). This study report of prescribing practices in the teaching hospitals of the country are found to be unsatisfactory and antibiotic resistance patterns against common microorganisms will inform physicians to practice their rational use.

Keywords: Rational use of antibiotics, antimicrobial resistance, culture and sensitivity test

Introduction:

Teaching hospital is an ideal place for a proper health service delivery center to control patient's infection by rational antimicrobial therapy. Appropriate antibiotic use improves patient's outcomes and prevents the emergence of antibiotic resistance. But irrational antibiotic practices cause the development of antimicrobial resistance which poses a serious threat to human health and welfare and undermines national economies worldwide. Annual losses stemming from antimicrobial resistance are estimated to range from 21000 million to 34000 million dollars in the United States of America and about 1500 million Euros in Europe (Infectious Disease Society of America and European Commission, 2011). According to a recent study in Thailand, in 2010, antimicrobial resistance was responsible for at least 3.2 million extra hospitalization days and 38 481 deaths, and for losses amounting to 84.6–202.8 million United States dollars (US$) (Pumart *et al* .2012). Though antibiotic resistance is a serious global problem, no organized initiative is taken about this in our country.

With reviewing these data and lack of local study to control antibiotic resistance development, a teaching hospital like BIRDEM general hospital was selected as a hospital that plays a key role in the development of antimicrobial resistance. Appropriateness of antimicrobial therapy to the admitted patients was evaluated by the department of microbiology for identification of targets of quality improvement in antibiotic prescription patterns. Our hospital antibiotic surveillance was an attempt to improve patient's outcome whilst reducing adverse effects associated with antimicrobial use which has been widely implemented in the developed countries and found fruitful (MacDougall *et al*. 2005).

Material and methods:

An observational and prospective study was designed to evaluate the appropriateness of the patient's antibiotic prescriptions of six month duration and was carried out from September'12 to March'13 at BIRDEM General Hospital, Dhaka, a 700 — bed teaching hospital in the capital city of Bangladesh with the ethical approval of Ethics Review Committee of BIRDEM and informed consent from all participants and facilities involved in the study. Junior doctors collected data from the hospitalized randomly selected 336 patients suffering from infection and treated them especially with antibiotics of all four main medical specialties from the medical record file and by interview.

Data collectors noted the points on a predesigned questionnaire. The information included patient's socio-demographic characteristics, clinical presentation at admission, reports of routine investigations, culture and antibiotic sensitivity tests and the pattern of antibiotic prescription. Special attention was given to noting the route, dose and duration of antibiotic administration and whether it was given at hospital admission or it was related with or without clinical evidence of infection and whether based on with or without microbial culture and sensitivity test results.

In the present study, WHO guidelines were taken into consideration with a few modifications for evaluating the rationality of the antibiotic prescriptions (WHO,1992). The parameters for evaluation were: (1) Indication of infection (2) Diagnosis of infection (3) Appropriate selection of antibiotic (4) Choice of regimen — dose, route and duration of therapy. Dose and duration of antibiotics were not the same in all patients as severity of infection varied from patient to patient with the same type of disease with complications or without complications, with comorbid, compliance, nontoxic and well hydration etc. For this reason, during spot data collection, information on dose and duration was not recorded.

Results:

Prescription of antibiotics: The survey revealed on admission to hospital antibiotics were prescribed to 48% (**Fig. 1**) patients and 63.1% of patients were treated with antibiotics without confirmatory diagnosis by laboratory investigation.

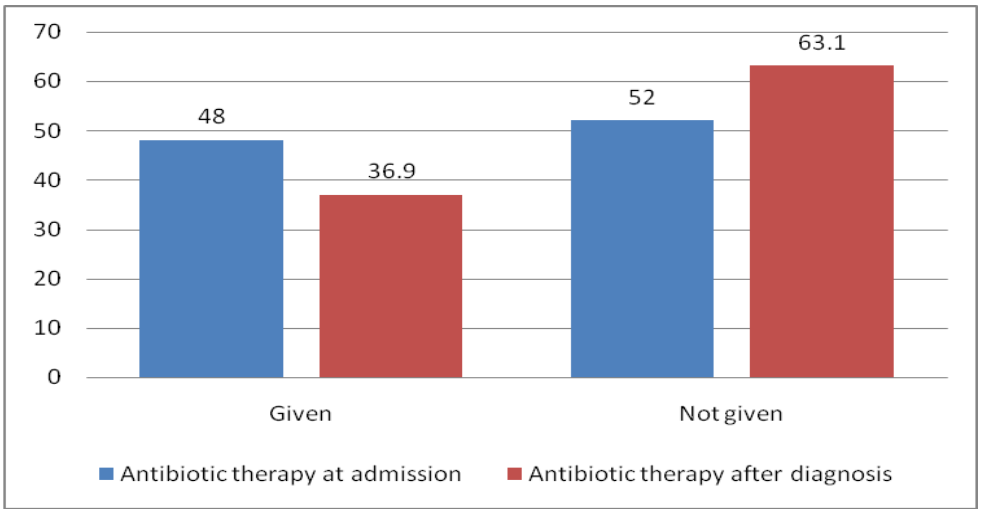

Fig. 1: Bar diagram showing antibiotics therapy at admission after diagnosis and without diagnosis

In this study we also demonstrated the pattern antibiotic prescription. On clinical diagnosis of infection most of the (95.8%) patients were prescribed (84.2%) antibiotics (**Fig. 2**).

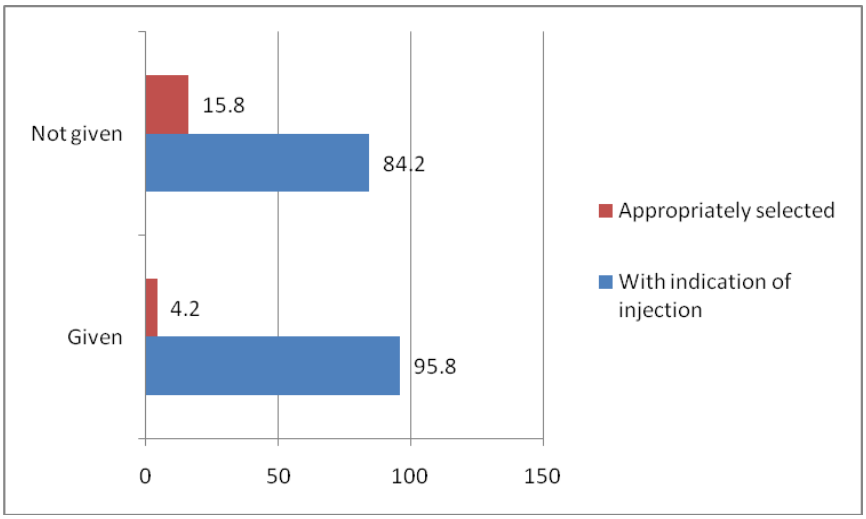

Fig. 2: Bar diagram showing appropriateness in antibiotic prescription with or without an indication of infection and its selection.

We have represented the variations in the mode of antibiotic administration. The maximum (61%) studied patients received single antibiotics and mostly (94.6%) by parenteral route (**Fig.3**).

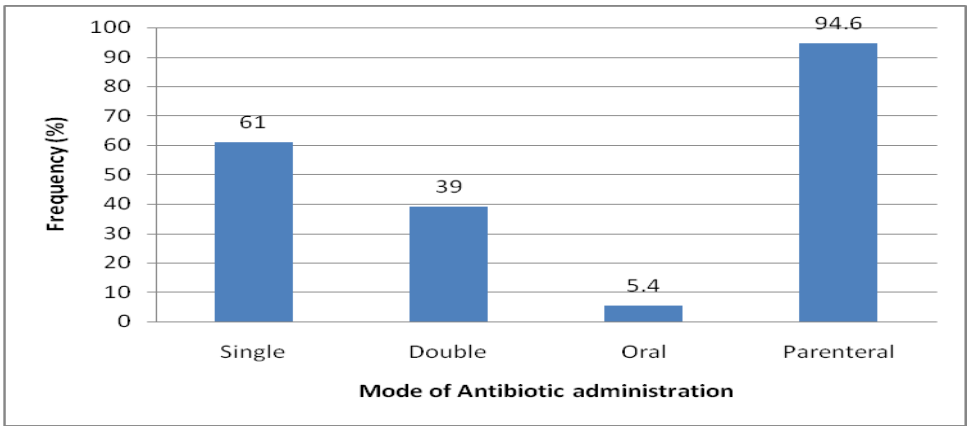

Fig. 3: Bar diagram showing the proportion of single and multiple antibiotic therapy and the ratio of oral and parenteral antibiotic administration.

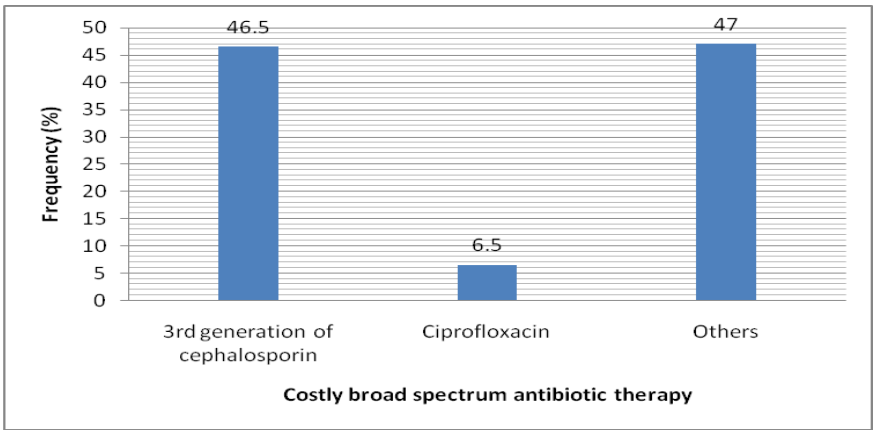

Fig. 5: Bar diagram showing costly and broad spectrum antibiotic therapy

The figure number 5 reveals the most commonly prescribed antibiotics were third generation of cephalosporin to more patients (46.5%) than that of cheap and oral ciprofloxacin to only 6.5% patients**.**

Cultural examination and pattern of antibacterial resistance:

Bacteriological investigation done only in 36.9% patients and 43% (**Fig. 4**) cases has yielded growth and the Table 1 reveals the growth of *E. coli* (26.4%), *Staph aureus* (24.5%) and *Pseudomonas* (20.7%) species as the most commonly isolated pathogens.

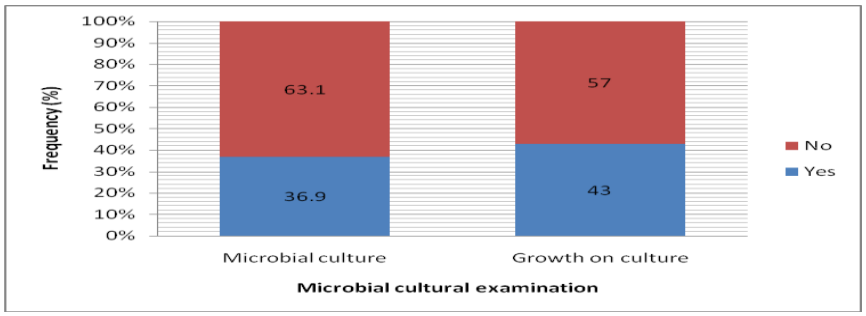

Fig. 4: Bar diagram showing proportion of bacterial growth and no growth on culture

Table -1: Summarizes the frequency of single and multidrug resistant microbial isolates from patient's clinical specimens of BIRDEM General Hospital (percentage in parentheses).

Single drug resistant bacteria	Hospital	Multidrug resistant bacteria	Hospital
E. coli	14 (26.4)	ESBL positive *E. coli*	3
Staphylococcus aureus	13 (24.5)	ESBL positive *Enterobacter*	1
Pseudomonas aeruginosa	11 (20.7)	ESBL positive *Acinetobacter*	1
Klebsiella sp.	6	ESBL positive *Citrobacter*	1
Proteus	4	MRSA	2
Total - 56			

The figure number 5 showed variation in antimicrobial resistance of *Pseudomonas aeruginosa*. The resistance pattern showed that 72.8% were resistant to ceftazidime, ciprofloxacin and imipenem, 63.6% to amikacin and 81.8% to pipercillin.

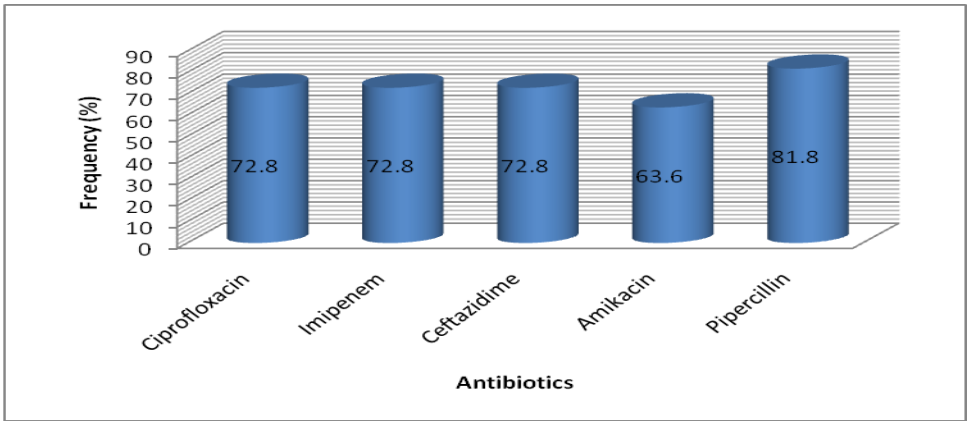

Fig. 5: Bar diagram showing pattern of anti-pseudomonal resistance

Maximum isolated and identified pathogenic bacterial antimicrobial-resistance is shown in **Fig.6.** *E. coli* is found to be more resistant than *Staphylococcus aureus* to commonly used antibiotics like ceftriaxone (64.30%: 61.5%), ciprofloxacin (78.6%: 38.5%), gentamicin (50%: 30.8%) and Trimethoprim + Sulfamethoxazole (64.30%: 54.9%) in patients.

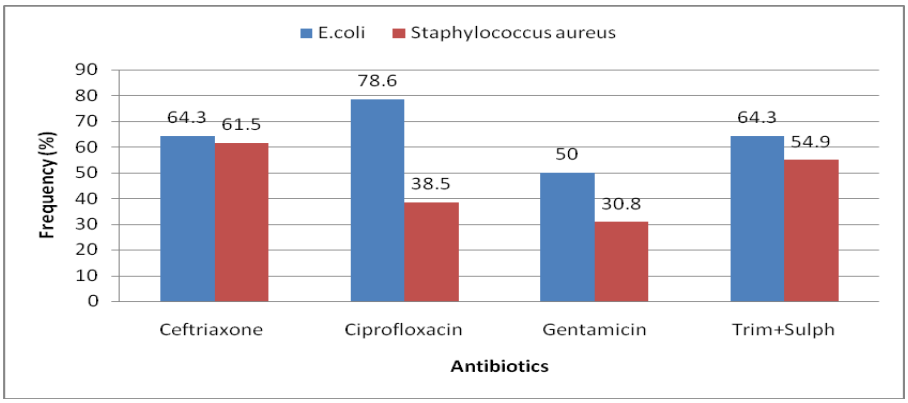

Fig. 6: Bar diagram showing variation in antimicrobial resistance to common pathogenic bacteria

Discussion:

Prescription of antibiotics:

This cross-sectional observational study estimates the magnitude and quality of rational antibiotic prescriptions in the teaching hospital. The study result is an invaluable tool required to update treatment methodologies for medical students. On the other hand, this surveillance enables effective patient care through appropriate antimicrobial

selection, particularly for empirical antimicrobial selection. Careful monitoring, analysis, and understanding of pathogen resistance can be important for the initiation of the prudent and appropriate use of antibiotics in hospitalized patients.

The findings of this study illustrated patterns of empirical antibiotic use in the hospital. Empirically, antibiotics were prescribed to 48% of patients on admission to hospital (**Fig. 1**).A similar study of KSA shows the empirical prescriptions in more patients (58.7%) than other types of prescriptions (Ashmony 2013). This empiric treatment of infections with a reasonably well-defined clinical presentation is more likely to be appropriate than that of infections with an undifferentiated presentation. This large number of patients empiric therapy is justified as the microbiology department of this hospital disseminated bacterial resistance patterns or antibiograms for important pathogens according to general principles of antimicrobial therapy (Thompson *et al.* 1998)

Selecting appropriate antibiotic regimen for patients with bacterial infections has an important role in controlling infection. In our study, 95.8% (**Fig. 3**) patients were given antibiotics on only clinical diagnosis of infection. A similar study in India found 56.75% of prescriptions were based on symptoms rather than the diagnosis (Bhavesh *et al.* 2012). Our study pointed out that antibiotics were prescribed to 63.1% of patients without confirmatory diagnosis (Fig. 2). There is every chance of misuse of antibiotics in these undiagnosed cases, which will lead to the development of antimicrobial resistance. Similarly, a study which was carried out in Yemen (2012) showed about 68.18% of all medical prescriptions was without diagnosis and physicians prescribe antibiotics without a culture sensitivity test in percent of cases (Ashmony, 2013). Hart (1998) conducted a survey among rural medical practitioners with an average of 11 years' experience showed 60% of antibiotics prescriptions on the symptoms alone (Hart *et al.* 1998).

The present study revealed that 61% of the surveyed patients were receiving one antimicrobial agent (**Fig. 3**). A similar study of KSA found 42.2% of patients were prescribed a single antibiotic, whereas combination therapy was given to 30.2% of the patients (Ashmony, 2013). Khan S. studied the same issue in Pakistan (2013) and found 10%, 67.50% and 22.5% patients were prescribed single, double and triple antibiotics respectively (Khan et al.2013) . The results of the combined therapy are comparable to those in the previous study of Turkey, showing 39.8% were receiving one drug, 42.8% two drugs, 12.1% three drugs. This high proportion of combination therapy may be related to the prescription of empirical treatment without the support of microbiological test results in order to increase the spectrum of action.

Routes of administration were also investigated in the specialized diabetes hospital, with 94.6 % receiving parenteral therapy against 5.4 % who had received oral antibiotic therapy (**Fig. 3**). In some cultural settings, antimicrobials given by injection are considered more efficacious than oral formulations. This tends to be associated with the over prescribing of broad spectrum injectable agents when a narrow spectrum oral agent would be more appropriate (Ceyhan *et al.* 2010).

The use of a commonly prescribed antibiotic is a major contributor to the development of drug resistance and its spread in hospitals. The current survey reveals (Fig. 5) the most commonly prescribed antibiotics were third generation of cephalosporin to more patients (46.5%) than that of cheap and oral amoxicillin + clavulanic in 7.8% and ciprofloxacin to only 6.5% patients. Other studies have shown that the penicillin group is the most commonly prescribed to 42% of patients in Arar central hospital of KSA, followed by cephalosporins 25.66% (Gumodoka *et al*. 1996). In point prevalence study performed at 15 hospitals in Italy, penicillin and cephalosporins were the most frequently used antibiotics (Shehab *et al.*2013).

A similar survey was conducted in Turkey in a research hospital; when antibiotics used with the aim of treatment were taken into consideration together with prophylactic use, the most commonly used class of antibiotics was penicillin and the latest generation of cephalosporins (Porretta *et al.* 2003).

Cultural examination and pattern of antibacterial resistance:

The study pointed out that bacterial culture of patient's clinical specimens has yielded the growth of etiologic pathogens in only 43% (**Fig. 7**) cases.

This less number of isolation in bacterial culture proves that the prescription of antibiotics prior to diagnosis was according to regular communique with clinical microbiologists on antimicrobial sensitivity pattern.

Pseudomonas aeruginosa has the inherent property of developing resistant. Hence, it is necessary to know the current resistance pattern for proper use of anti-pseudomonal agents. In our study, *Pseudomonas aeruginosa* was isolated (Table-1) in 20.7% cases and its resistance pattern (**Fig. 8**) shows more resistant to pipercillin (81.8%) than that of all other four antibiotics as in ceftazidime, ciprofloxacin and imipenem (72.8%) and to amikacin (63.6%). A central Indian study (2007 to 2010) 24% resistant to Amikacin (Yilmaz *et al*. 2009).

A similar study in China (2011) shows resistant to pipercillin (54.1%), ceftazidime (48.4%), ciprofloxacin (52.8%), and imipenem (43.4%) and to amikacin (29.6%) (Chaudhar *et al*. 2013). Carbapenems such as imipenem are the last resort of drugs for the treatment of MDR pathogens including *P. aeruginosa* but in our study revealed they are highly resistant to it. Resistance to carbapenems, which is often accompanied by resistance to multiple other agents, has increased in all parts of the world (Xu *et al*. 2013).

Maximum isolated and identified pathogenic bacterial antimicrobial-resistance is shown in Fig. 9. E. coli were found to be more resistant than *Staphylococcus aureus* to commonly used antibiotics like ceftriaxone (64.30%: 61.5%), ciprofloxacin (78.6%: 38.5%), gentamicin (50%: 30.8%) and Trimethoprim + Sulfamethoxazole (64.30%: 54.9%) but less resistant to ceftazidime (57.1%: 69.2%). A similar study of T. Yasmin (2012) shows 61% *E. coli* resistant to ceftazidime (Shigemi *et al*. 2009). It correlates with the study done by Sasirekha *et al.* (2010) and Singh and Goyel (2003) in India where they found 85% *E. coli* resistant to ceftazidime (Yasmin 2012).

Conclusion:

Prevalence surveys proved to be useful tools to judge the appropriateness of AMT and to identify determinants of inappropriate use. This study showed that in a setting with a low use of AMT, there were few patients who inadvertently did not receive AMT. On the other hand, a substantial number of the patients were treated inappropriate. However, the findings of the present study, based on the analysis of the micro-sample of prescriptions, warrant cautious interpretation. Despite the proven value of antibiotic stewardship in controlling antibiotic resistance in hospitals, more insight into its implementation is needed in order to explore patterns of antibiotic prescribing.

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Authors' Contributions:

The authors confirm contribution to the paper as follows:

- Study conception, designing and writing the draft manuscript by Abdullah Akhtar Ahmed
- Data collection by Kaniz-E-Zannat, Sufana Shikder, Nusrat Jahan and Anta Melan
- Analysis and interpretation of results by Razib Hasan and Nusrat Akhtar Jui
- Supervised the work by L. Barai

All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest: The authors declared that they have no conflict of interest.

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