

Antimicrobial resistance and related issues: An overview of Bangladesh situation

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Article Info

Received: 7 May 2014

Accepted: 8 May 2014

Available Online: 11 May 2014

DOI: 10.3329/bjp.v9i2.18831

Cite this article:

Rahman MS, Huda S. Antimicrobial resistance and related issues: An overview of Bangladesh situation. Bangladesh J Pharmacol. 2014; 9: 218-24.

Abstract

The present study was designed to understand Bangladesh situation about antimicrobial resistance. Half of the *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas* and *Klebsiella* showed resistance against older and common antimicrobials. Most (50%) common reasons to prescribe antimicrobial are fever, respiratory and urinary tract infection. About 70% prescriber mentioned diagnostic uncertainty and emergence of resistance as causes for increase in antimicrobial prescribing. 51.9% of prescribers opined that physicians prescribe antimicrobial more than the actual need. About two-third of 5th year medical students answered correctly on different issues related to antimicrobials and resistance. Antimicrobial and resistance received little emphasis in Pharmacology and Microbiology written questions at both undergraduate (0.7 to 16.1%) and postgraduate (0.9 to 18.4%) level. Print (0.02 to 2.0%) and electronic media (0.0 to 0.6%) attaches small importance on the issues. Nothing related to 'antimicrobials' and 'measure to contain resistance' were mentioned in related policy documents.

Introduction

Different studies conducted in Bangladesh during last decade revealed that there is polypharmacy, high use of antimicrobials, vitamins and injectables in hospitals and very low generic prescribing (Rahman et al., 1998; Islam et al., 2007; Chowdhury et al., 2008; Das and Rahman, 2010; Holloway, 2010). Moreover, inadequate access to effective antimicrobials, incomplete therapy and though occasional but questionable quality of medicine negatively contributed in emergence of resistance (Okeke et al., 1999; WHO, 2000; Faiz and Basher, 2011). Antimicrobial resistance is a mounting threat to the control of infectious diseases both globally as well as locally in Bangladesh. During last seventy years, development of effective antimicrobials had reduced incidence of life-threatening infections, however that achievement has been eroded by the emergence of resistance (Shnayer-son and Plotkin, 2002). Microbes developed resistance primarily in the hospitals, however that later spread in

the community imposing more risk to the human health. Infections with resistant microbes not only result in greater morbidity and mortality, but also increase the health care costs. The loss of effectiveness of the antimicrobials leads to longer duration of research as well as increased development expenses (Levy, 2002).

Against this background, attempt has been taken, to overview the status of antimicrobial resistance and related contributory issues in Bangladesh. Evidences were gathered on sensitivity pattern, emphasis on antimicrobial related issues in teaching-learning activities in medical and general education, emphasis on related issues in electronic and print media, understanding of the medical students on related issues and perception of prescribers regarding antimicrobial prescribing. Moreover, to obtain a detail picture, medicine related policies and regulations were analyzed.



Materials and Methods

Sensitivity pattern of the microbes isolated in different institutions

Information on antimicrobial sensitivity pattern of *Escherichia coli*, *Staphylococcus aureus*, *Pseudo-monas* and *Klebsiella* isolated in the Department of Microbiology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh Medical College, Ibrahim Medical College and Rajshahi Medical College during the period from July 2010 to December 2010 was collected from the departmental records. The collected data were cleaned, synchronized and compiled in a common table, which was analyzed later.

Understanding of medical community on antimicrobial resistance

Study among physicians

Questionnaire survey was conducted among physicians of different institutions during March 2011 on clinical conditions leading to antimicrobial prescribing, perceived factors that increase antimicrobials prescribing and opinion regarding statement "physicians prescribe antimicrobial more than they actually need".

Study among 5th year medical students

Questionnaire survey was conducted among 5th year medical students of different medical colleges during March 2011 regarding different aspects on antimicrobial related issues. A questionnaire was prepared on 'antimicrobial spectrum', 'clinical use', 'theory on resistance'. The respondents were asked about the diseases for which they have taken antimicrobials and the name of the antimicrobial taken in last six months. In addition, whether the antimicrobials were taken according to qualified physicians or not were enquired and in case of positive response, the respondents were asked about whether the course was completed or not.

Emphasis on antimicrobial resistance in teaching-learning activities of medical institutions

Undergraduate: All available questions on Pharmacology and Microbiology of 2nd Professional MBBS examinations held between January 2006 and July 2010 in all universities of Bangladesh were included. Questions on 'antimicrobial' and 'resistance' were identified and labeled by the qualified pharmacologists on the principle of conceptual mapping. Marks allocated for the designated question was then recorded. Proportion of marks allocated was calculated on the basis of total marks mentioned in the questions.

Postgraduate: All available questions on Pharmacology and Microbiology for MD and MS examinations of different disciplines held in all universities of Bangladesh (January 2006 to July 2010) were included. Questions on 'antimicrobial' and 'resistance' were

identified and labeled by the qualified pharmacologists on the principle of conceptual mapping. Marks allocated for the designated question was then recorded. Proportion of marks allocated was calculated on the basis of total marks mentioned in the questions.

Emphasis on antimicrobial resistance in general education

Textbooks on science and related disciplines of class VI to class XII were analyzed using conceptual mapping in order to calculate the emphasis on 'health', 'drug', 'antimicrobials'/'antibiotics', 'resistance'. Similarly, Biology questions papers of the Secondary School Certificate (SSC) examinations held from 2006 to 2010, Botany and Zoology question papers of the Higher Secondary Certificate (HSC) examinations held from 2006 to 2010 were also analyzed.

Emphasis on antimicrobial resistance in print media

Four daily newspapers were selected [two Bengali and two English] and they were collected for the month of March 2011. The total area of the newspapers was measured in sq inch including the news, features, magazines and advertisements. The news or features were categorized and labeled into 'health', 'drug', 'antibiotic' and 'resistance', which were measured in sq inch to be expressed as percentage of the total area of the newspaper.

Emphasis on antimicrobial resistance in electronic media

Three television channels [Channel I, Banglavision and Ekushey Television] were selected for the study. The 'health', 'drug', 'antibiotic' and 'resistance' related news or features were calculated in hours to be expressed as percentage of the total hour broadcasted.

Policy analysis

'National Health Policy 2010', 'National Drug Policy 2005', 'Drug (Control) Ordinance 1982', 'Bengal Drug Rules 1946' and 'Bengal Drug Act 1940', were collected (either hard copy or electronic version). These documents were searched by key words 'antibiotic', 'antimicrobials', 'rational', 'dispensing', 'prescribing', 'resistance', 'over the counter'. If the searched word was present, it was marked manually.

The methodology of studies and tools of data collection was validated. The data on different issues related to antimicrobial resistance at different levels were assessed. Input were received from the related experts, particularly regarding methodology was appreciated.

Results

The sensitivity pattern of *E. coli* shows that this microbe is about 40% sensitive to ciprofloxacin, ceftazidime,

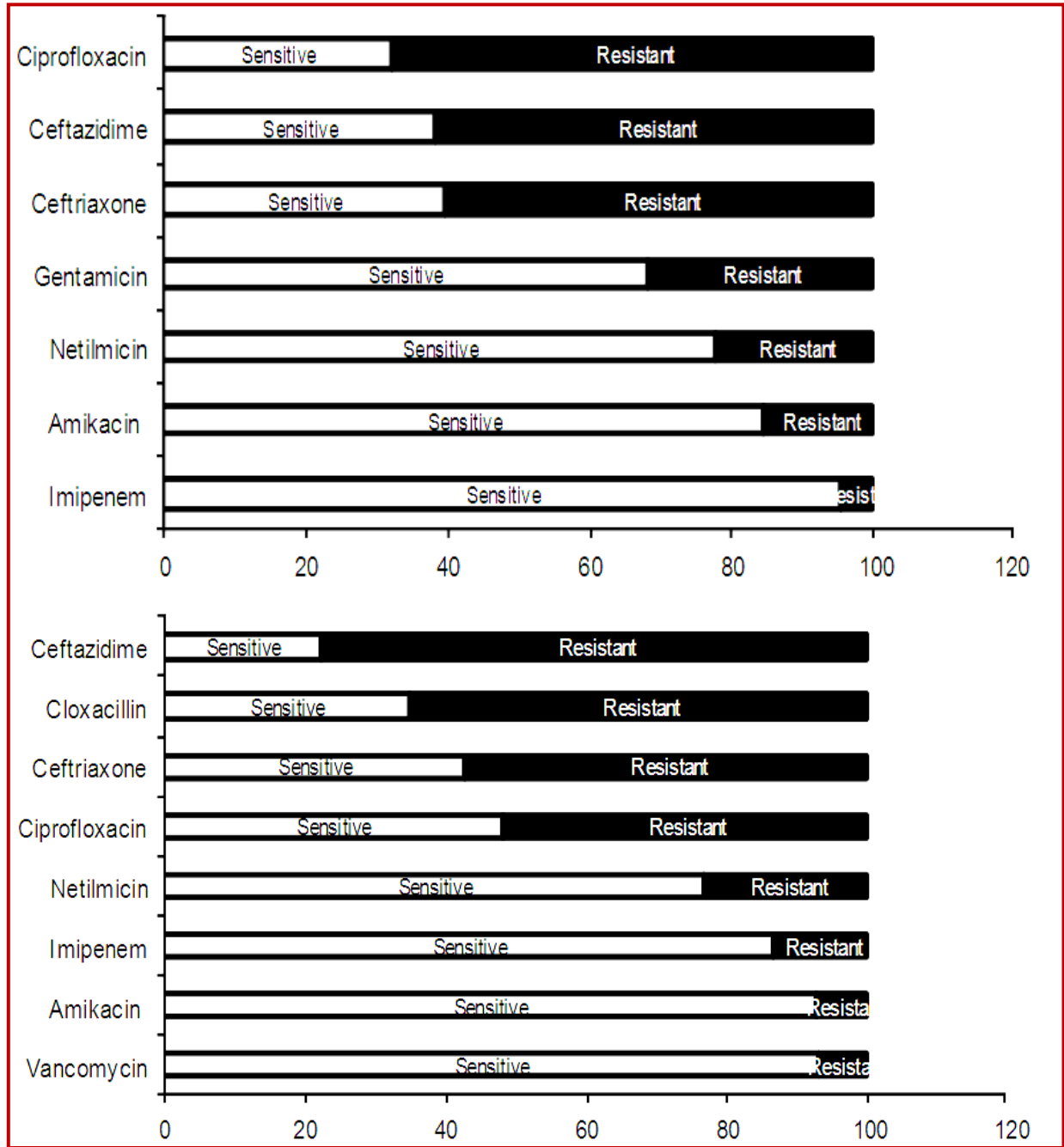


Figure 1: Antimicrobial sensitivity pattern of *E. coli* (n = 1293; Upper), *S. aureus* (n = 114; Lower)

ceftriaxone and about 90% sensitive to amikacin and imipenem (Figure 1). The results of *S. aureus* shows that, they are about 30% sensitive to ceftazidime, about 40% sensitive to cloxacillin, ceftriaxone and about 95% sensitive to amikacin and vancomycin (Figure 1). The sensitivity pattern of *Pseudomonas* reveals that they are almost 30% sensitive to ceftazidime and ceftriaxone, about 50% sensitive to netilmicin, ciprofloxacin and almost 95% sensitive to imipenem (Figure 2). The sensitivity picture of *Klebsiella* is about 40% sensitive to ceftriaxone, ciprofloxacin, 80% to amikacin, imipenem

and almost 95% sensitive to azithromycin (Figure 2).

According to the physicians of different institutions, most of them (about 50%) prescribe antimicrobials in respiratory tract infection, fever and urinary tract infection. Few (about 10%) prescribe in otitis media, dysentery, septicemia (Table I). Majority of them (about 70%) pointed out that diagnostic uncertainty and emergence of resistant microbes are the main causes for increase in antimicrobial prescribing. It is also mentionable that 16.4% of them prescribe antimicrobials as

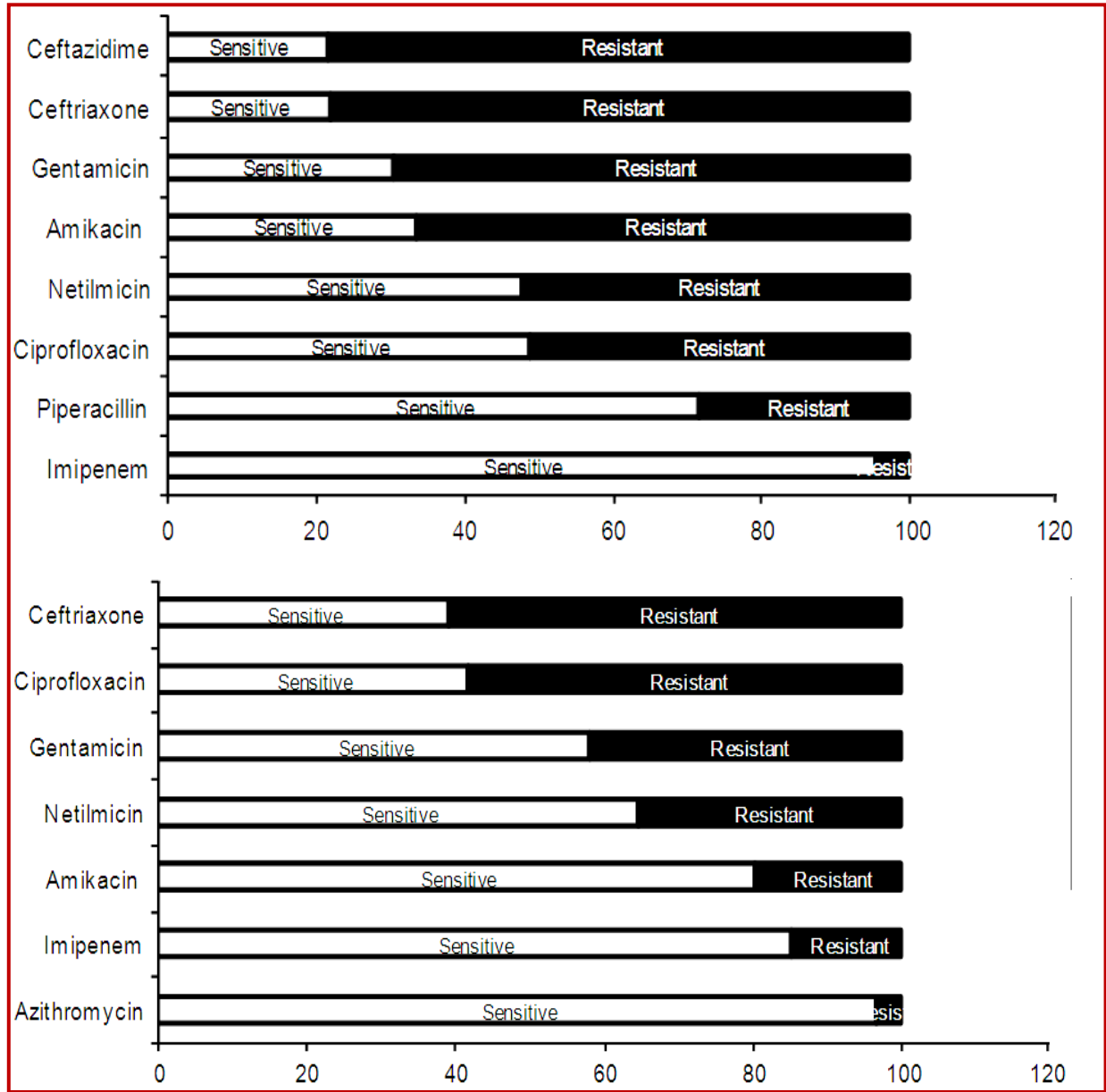


Figure 2: Antimicrobial sensitivity pattern of *Pseudomonas* (n = 225; Upper), and *Klebsiella* (n = 171; Lower)

there is possibility of losing patient (Table II). Over all 51.9% physicians agreed with the statement, "Physicians prescribe antimicrobial more than they actually need"; whereas 24.8% disagreed with the statement.

In survey conducted on 5th year medical students, about 71.3% of them answered correctly on clinical use of antimicrobials, 67.3 and 57.9% answered correctly about 'theory on resistance' and 'antimicrobial spectrum' respectively. While enquired about reason of taking antimicrobials in last 6 months, 23.8, 24.8, 23.9 and 12.1% of the students mentioned fever, sore throat, diarrhea and RTI respectively as their reason. Due to these reasons, the students had taken different antimicrobials like- azithromycin (67%), ciprofloxacin

(48%), amoxicillin (30%), metronidazole (25%), cefradine (20%), flucloxacillin (10%) and others (31%).

Among the students, 76.0% took antimicrobials according to prescription of qualified physicians, 15.7% took antimicrobials not prescribed by physicians and 6.4% were not sure about the issue. The students who took antimicrobials as prescribed by qualified physicians, 80.2% completed the course, and the remaining (19.8%) stopped taking the antimicrobial before completion of course.

The emphasis on antimicrobial and resistance in written questions of Pharmacology and Microbiology of MBBS examinations were evaluated. It was revealed that, in Pharmacology 16.1 and 0.8% questions covered anti-

Common conditions for which graduate physicians prescribe antimicrobials	
Clinical condition	Proportion of physicians mentioned (n = 214)
Respiratory tract infection	57.9 (124/214)
Fever	54.2 (116/214)
Urinary tract infection	50.9 (109/214)
Postoperative infection	36.9 (79/214)
Meningitis	32.2 (69/214)
Diarrhea	12.2 (26/214)
Otitis media	11.7 (25/214)
Dysentery	11.7 (25/214)
Speticemia	11.7 (25/214)
Sore throat	5.1 (11/214)
Others	88.3 (189/214)

microbial and resistance respectively, whereas in Microbiology 1.6 and 0.7% questions covered antimicrobial and resistance respectively.

The emphasis on antimicrobial and resistance in written questions of Pharmacology and Microbiology of MS and MD examinations were evaluated. In Pharmacology compartment of different MS examinations, 18.4% questions were on antimicrobial and 1.2% on resistance. In different MD examinations, 13.3% questions were on antimicrobials and 1.2% on resistance. In Microbiology compartment of different MS examinations, the scenario is, 1.4% questions were on antimicrobial and 2.1% on resistance. In different MD examinations, 0.9% questions were on antimicrobials and 0.9% on resistance.

In general education, emphasis on health awareness, microbes, antimicrobial and resistance in books from class VI to class XII had ranged between 11 to 69% on health awareness and 7 to 38% on microbes. However, there is no (0%) coverage on antimicrobial and resistance. In Botany and Zoology questions papers of SSC and HSC examinations, 10.3 to 17.3% questions cover microbes, 0.9 to 2.5% on antimicrobials and no questions on resistance.

In print media, coverage of health, drug, antimicrobial and resistance in newspaper shows that, 0.5 to 2.0% area covers health related features and news; out of which, 0.0 to 0.5% covers drug related features and news. There was no coverage in features and news on antimicrobial and resistance related issues.

In electronic media, 0.4 to 0.6% time of the total duration of program was on health related issues, 0 to 0.02% of total time duration was on drug related programs. Only one channel broadcasted a program on antimicrobial and resistance for one hour, which covered 0.01% hour of the total time of broadcasting.

Factors identified by physicians that increase anti-microbials prescribing	
Factors	Proportion of physicians mentioned (n=214)
Diagnostic uncertainty	73.8 (158/214)
Emergence of resistant microbes	72.0 (154/214)
Earlier treatment by quack	52.3 (112/214)
Lack of information about sensitivity pattern	49.1 (105/214)
Concern about cost of sensitivity testing	48.1 (103/214)
Patient request/expectation/satisfaction	34.6 (74/214)
Time constraint	30.4 (65/214)
Promotion of newer antimicrobials	21.5 (46/214)
Concern about cost of return visit	20.1 (43/214)
Possibility of losing patient	16.4 (35/214)

In the studied policy documents on health and medicine, nothing related to 'antimicrobials' and 'measure to contain resistance' were mentioned.

Discussion

The link between inappropriate use of antimicrobials and development of antimicrobial resistance was acknowledged in different scientific studies and global proceedings (WHO, 1998; 2002). In Bangladesh, prescribers generally diagnose microbial infection on clinical judgment and select antimicrobial on empirical basis (Faiz and Rahman, 2004), which unfavorably affected the sensitivity pattern of microbes. Moreover, reluctance of the lawmakers and regulators to enact law to overcome inadequacy in rules and regulation to control antimicrobial prescribing and dispensing led to worsening of the situation.

Antimicrobial sensitivity pattern reflects the emergence of resistance against common antimicrobials, which are similar with that of the previous studies (Okeke et al., 2005; Rahman et al., 2007; Akond et al., 2009; Rogers et al., 2011). Though antimicrobials like ciprofloxacin, ceftazidim and ceftriaxone have become ineffective because of emergence of resistance, the microbes are still sensitive to imipenam, azithromycin, vancomycin and amikacin. This pattern of sensitivity does not correlate with the previous findings (Hasan et al., 2011). Prescribers mentioned diagnostic uncertainty and emergence of resistance as major causes of prescribing antimicrobials, though some of them mentioned possibility of losing patients as one reason.

Antimicrobial and resistance received very little importance at the undergraduate level (MBBS) in the course

and examinations of Pharmacology and Microbiology subject. Whereas, at postgraduate level, portion of the MD and MS postgraduate curricula also represent similar picture. The emphasis on antimicrobials was similar in the previous study conducted at undergraduate level (Begum et al., 1999). Medical education of Bangladesh was not adequately addressing the impending health issues of the country, which was discussed earlier and some changes were suggested (Rahman, 1995a; Rahman, 1995b). There was innovative effort to improve the relevance of the course content and required prescribing skill of the future medical graduates (Rahman et al., 2000). Recent undergraduate medical curriculum (BMDC, 2012) has incorporated some of the recommendations of previous studies, which might contribute positively in near future.

In case of general education, microbes are taught at SSC and HSC levels in Botany and Zoology subjects. Though, antimicrobials and resistance are not receiving any importance, which should be taught and evaluated in the SSC and HSC levels under any relevant subject. People become aware about different issues through learning from different sources including lay media. The antimicrobial related issues received negligible emphasis in different print and electronic media, indicating little awareness among the key anchors of health programs and news editors of health pages regarding antimicrobials related issues and its implications.

Inadequate information was available about these issues beforehand in Bangladesh. Through this study, a quick overview of the situation was done and a number of evidences on status of the issue in different spheres of life were gathered. In addition, comprehensive information was obtained on sensitivity pattern of microbes, emphasis of antimicrobial resistance in different teaching-learning activities, print and electronic media. In spite of having an excellent National Drug Policy formulated in 1982, which was updated later in 2005, nothing was mentioned as directives and regulation in any of the antimicrobial related policy documents. The clarity of understanding about the status of antimicrobial resistance and the perceived influencing factors is essential to take initiative to contain emergence of resistance. The findings of the present study will form the conceptual basis of initiatives directed towards containing emergence of bacterial resistance.

“War is too important to be left to the generals,” as paraphrased in Clemenceau and the Third Republic (Jackson, 1946). The struggle of human to conserve the effectiveness of antimicrobials against microbes is so complicated that require concerted effort of number of experts. In this context, war against microbes is too important to be left to the clinicians. There are too many aspects of infection management that are out of the scope and training of the clinician. Therefore, pharmacologists, microbiologists, epidemiologists and molecu-

lar biologists all must participate in a concerted effort to design sound strategies to contain antimicrobial resistance by using antimicrobials scientifically to manage infectious diseases. The present study was just a preliminary and quick assessment, which formed the foundation of future researches.

Acknowledgement

The principal author gratefully acknowledges the financial support received from World Health Organization on the eve of World Health Day 2011 to conduct the study. The author also likes to express gratitude to the teachers of the participating departments of different institutions for their generous support and help and especially to the students of the Department of Pharmacology, BSMMU who worked hard for the study.

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