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Cephalosporin-3G, Highly Prescribed Antibiotic to Outpatients in Rajshahi, Bangladesh: Prescription Errors, Carelessness, Irrational Uses are the Triggering Causes of Antibiotic Resistance

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ABSTRACT

The study aims to assess the prescribing practices of antibiotics to outpatients attending public-private hospitals in Bangladesh and to investigate how the irrational uses of antibiotics influence the development of antimicrobial resistance in pathogens over time. A cross-sectional survey was conducted on 1100 prescriptions by interviewing outpatients at the exit point and at retail pharmacies. Infections in male patients (67%) were greater than female (32%). Unexpectedly 22% of patients visited quack doctors (unauthorized doctors), 32% did not complete antibiotic courses, and 10% took multiple antibiotics. As prescription errors the directions for antibiotic use were incomplete in 40% of cases and in a few cases, dosage form information was incomplete (17%) and absent (5%). The disease recovery rate was 12%, although no diagnostic test was performed in the majority (73%) of cases and no comments about disease recovery were in 81% cases. Post-operative infection was commonly found which could preferably be treated with rarely used antibiotics of DNA- or protein-synthesis inhibitors. Rarely used antibiotics (0.18–2% of prescribed antibiotics) were 1GCs, amoxicillin, co-amoxiclav, gatifloxacin, pefloxacin, and sparfloxacin. Most frequently prescribed antibiotics were cephalosporins (34%) followed by quinolones (16%), metronidazole (15%), macrolides (13%) and penicillins (7%). 3GCs (ceftriaxone, cefixime, ceftazidime), ciprofloxacin, azithromycin, and flucloxacillin were highly prescribed drugs in their respective groups. For better treatment, appropriate knowledge and practices regarding rational use of antibiotics need to be improved in patients and physician's level. Simultaneously drug authority should exercise power to control the misuse of antibiotics.

INTRODUCTION

Antibiotics are currently one of the most frequently prescribed drugs in hospitals worldwide. These drugs prescribed by the physicians have gained importance across the globe mainly because of an increase in antibiotic use, persistence of infections and drug resistance (Park, 2012; Okeke *et al.*, 2007; Remesh *et al.*, 2013). So the rational use of antibiotics is an important health concern. Irrational use, physicians' biases, unjustified self-medication, the random selling by pharmacists and patients' demands, lack of understating of antibiotic effectiveness strengthen the cost of therapy and rapid emergence of antimicrobial resistance in developing country including Bangladesh (Biswas *et al.*, 2014). In Bangladesh, antibiotics can readily be purchased without a prescription despite the existing laws prohibits such illegal practices. To protect the misuse of antibiotics, most of the countries have laws that prevent selling these medications in pharmacies without a medical prescription (Grigoryan *et al.*, 2007). In Bangladesh, most of the cases the patients do not maintain antibiotic regimen during the course of therapy as many physicians are prescribing antibiotics irrationally without taking consideration of the positive clinical microbial test (Sutradhar *et*

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al., 2014). Ultimately, this is an alarming situation of public health concern in Bangladesh where higher rates of resistant microbial strains emerge, superinfections ensue. Therefore, both efforts and resources are wasted affecting the total health care system (Okeke *et al.*, 2007).

To solve the problem concerning the misuse of antibiotics, the study of antibiotics usage pattern and its associated factors such as frequent monitoring, suggestions, evaluation, documentation, and publications of the trend of antibiotic prescriptions by the practitioners can help to make the physicians to be more professional and careful when antibiotics are prescribed to the outpatients (Shankar *et al.*, 2003). It is expected that a highly representative data on patients' knowledge, beliefs, attitude, and awareness concerning rational use of an antibiotic can aid the prescribers to reduce the illegal of antibiotics and the problem of microbial resistance. The control and regulation measures for the sale of antibiotics in developing countries are often insufficient that not only affect Bangladesh but also other developing countries throughout the world (Borg and Scicluna, 2002; Al-Bakri *et al.*, 2005; Mitsi *et al.*, 2005; Nakajima *et al.*, 2010). Therefore, research is needed to evaluate the specific antibiotic usage patterns in developing countries so that educational efforts on a national basis can be developed and implemented, such as public information campaigns, educational interventions, strict enforcement of over-the-counter drug availability, establishment of evidence-based clinical practices for doctors with regular medical audit and lastly, it is essential to share information about appropriateness of antibiotic use between health professionals and patients, together with strict implementation of the laws (Chan and Tang, 2006; Barah and Goncalves, 2010) to ensure that patients receive the best quality of health care.

The lack of minimal knowledge and misconceptions about antibiotic use have been reported in several studies among populations of both developed and developing countries (Nakajima *et al.*, 2010; Chowdhury *et al.*, 2013; Hasan *et al.*, 2009; Saha *et al.*, 2010; Fahad *et al.*, 2010). Here, the present survey-based study is designed to document the insight of the current knowledge and practices regarding the use of antibiotics by the individuals living in Bangladesh. Information obtained from this study will provide a further extensive understanding of the development and evaluation of health education and prevention of antimicrobial resistance. This study, therefore, aimed to explore how the antibiotics are irrationally used by the patients as well as to correlate the prevalence of prescribed antibiotics to the current trend of antimicrobial resistance in Bangladesh.

MATERIALS AND METHODS

Site survey and study design

Rajshahi city, a divisional headquarters of Bangladesh, has an estimated population of 853,000. Eight crowded and busy points of the city having many retail pharmacies, namely Katakhali bazaar, Binodpur Bazaar, Station Bazaar, Kazla, Talaimari, Vodhra, Shaheb Bazaar and Laxmipur were selected for data collection. A cross-sectional survey was conducted on outpatient prescriptions at these points using a standard questionnaire approved by the ethics committee. The questionnaire contained some basic variables. Data was collected by interviewing the patients. Informed consent was taken from patients before carrying out the interviews. In total, 1100 respondents were interviewed on types of doctors visited by the patients, effectiveness and awareness of antibiotic use, information on the dosage form, information about the direction for antibiotic use, the clinical test for prescribing antibiotics, completion of the full antibiotic course, patient's compliance, etc as shown in the supplementary file.

Data collection

Data were collected by trained data collectors (M. Pharm students) who conducted interviews of the outpatients at exit points of hospital/clinic outdoors using a standard questionnaire. Total 1100 participants were enrolled in the study conducted for one year period during October 2013 to September 2014. Data were also collected from the patients in front of retail pharmacies by random techniques. Data on patients' disease recovery were collected by the over phone contacts.

Ethical considerations

The study was followed as per the general guidelines (section 12) of the WMA declaration of Helsinki (WMA declaration, 2017) and the method of questionnaire approved by the Institutional Ethics Committee, University of Rajshahi. No samples were taken from- or no hazardous agents were used to-the human subjects involved in the study. As the human subjects only participated in the interview, therefore, the study did not require any further approval. All participants were informed of the background and aim of the study and advised that the personal data would not be disclosed to protect their privacy. Most of the participants gave their written consent and in some cases where the participants were elderly, illiterate gave verbal consents. In the case of verbal consent, a snapshot of prescription had been taken and recorded as soft- and hard-copies. All survey documents were stored and compiled with interviewers' signatures.

Statistical analysis

Descriptive statistics were applied to the collected data using Microsoft Excel software 2010. The results were finally expressed graphically as mean, percentages.

RESULTS

Epidemiology of outpatients

Antibiotics were ordered to about 54% and non-antibiotics to 45% of outpatients (Table 1). Non-antibiotics usually cover a wide range of drugs of various therapeutic effects. Therefore, a large number of patients (54.36%) suggesting antibiotics indicated that infections were the most common health problem in the study area. The prevalence of infectious diseases under the age of 16–30 years was higher (50%) followed by 0–15 years (25%) and 31–45 years (14%). Moreover, the case of infections in male outpatients (67%) was higher than that of female (32%). About 67% of patients visited MBBS doctors, 22% visited quack doctors (unqualified and unauthorized persons who use to sell bogus medicine to patients is hereafter termed as a quack), and 8% visited BDS doctors. Although the survey site was a metropolitan city in Bangladesh, unexpectedly a large number of patients (22%) visited quack doctors for their treatment. No doubt, this value will be higher in the village/city side.

Table 1: Prevalence of prescription antibiotics and patient demography.

Demographic characteristics	Responses	Frequency (n = 1100)	%
Types of the drug in prescriptions	Antibiotics	598	54.36
	Non-antibiotics	502	45.64
Patients' age (years) who are suggested antibiotics (n = 598)	0–15	152	25.42
	16–30	302	50.50
	31–45	88	14.72
	46–60	44	7.34
	>60	12	2.01
Patients' sex who are suggested antibiotics (n = 598)	Male	402	67.22
	Female	196	32.78
Types of doctors visited by the patients	MBBS	402	67.22
	Quack	135	22.58
	BDS	50	8.36
	Others	11	1.84

Table 2: Prescription and usage pattern of antibiotics.

Demographic characteristics	Responses	Frequency (n = 598)	Percentage (%)
Suggested antibiotics in prescription	Single antibiotic	537	89.80
	Multiple antibiotics	61	10.20
Information on the dosage form	Complete	465	77.76
	Incomplete	103	17.22
	Not mentioned	30	5.02
Information on the direction for antibiotic use	Complete direction	358	59.87
	Incomplete direction	240	40.13
Clinical test for prescribing antibiotics	With test	161	26.92
	Without test	437	73.08
Completion of full antibiotic course	Yes	411	68.73
	No	187	31.27
Patient's compliance	Disease recovery	74	12.34
	Noncompliance	36	6.02
	No comments	488	81.61

The usage pattern of antibiotics, demographics, prescription errors

Of patients who were prescribed antibiotics, about 90% were prescribed with single antibiotics and 10% with multiple antibiotics (Table 2). This result indirectly indicated that 10% of patients carried either superinfection or resistant bacterial strains since the doctors suggested a combined antibiotic therapy to them. Information about pharmaceutical dosage forms of prescribed antibiotics was found complete in 77.76% of cases, incomplete in 17% and absent in 5% of cases. In major cases (73%), doctors prescribed antibiotics without any diagnostic tests and in 40% cases, the complete directions for the use of antibiotic were absent. Such blind treatments usually allow pathogens to be shocked by antibiotics which might be the principal cause of the development of resistance in pathogens. Among the patients, the disease recovery rate was very low (12%) and in some cases (6%) prescribed antibiotics did not comply with the patients. Moreover, a large number of patients (81%) had no comments about disease recovery, which indicated that either the patients were bearing resistant pathogens or the prescribed antibiotics were less specific to the pathogens.

Antibiotic use in the community against diseases

Different antibiotics were found to be prescribed against a wide range of infectious diseases depending on their spectrum and severity (Table 3). The most extensively prescribed antibiotic was azithromycin, which was given against fifteen cases of diseases followed by ciprofloxacin (twelve cases), 3GCs (nine cases), 2GCs (eight cases), flucloxacillin (eight cases) and so on. But in most of the cases (73.08%) no antimicrobial tests were performed (Table 2). Therefore, the scenario obtained here was only the consequences of the physicians' biases and/or the market policy of pharmaceutical companies to a particular antibiotic. The prescribed antibiotics for POI were β-lactum group (penicillin

and cephalosporin) but cephalosporin resistance has been reported in many cities of developing countries (Bhattacharya *et al.*, 2011; Alvarez-Uria *et al.*, 2010; Breurec *et al.*, 2013; Reardon, 2014; Bharara *et al.*, 2015) including Rajshahi city, Bangladesh (Chouduri and Wadud, 2013; Chouduri and Wadud, 2014; Rashid and Rahman, 2014). Also recently in developed countries, cephalosporin resistance in gonorrhea has been reported (Kirkcaldy *et al.*, 2013). These evidences, therefore, suggested that POI should be treated with another group of antibiotics excluding β-lactum group.

Table 3: Prescription antibiotics against infectious diseases.

	Antibiotics	Reasons to see a doctor	Frq[1]
1.	**Cephalosporins**		
	1st generation[2]	Bronchial asthma, dental caries, POI[3], skin infec, toothache	5
	2nd generation[4]	Cold-fever, dysmenorrhea, ear infec, joint pain, nasal infec, priapism, POI Cesarean infec	8
	3rd generation[5]	Acne, cold-fever, ear Infec, gonorrhea, joint pain, POI, pneumonia, skin Infec, tonsillitis, UTI, nonspecific abdominal pain, cholelithiasis, leg injury	9
	4th generation[6]		0
2.	**Macrolides**		
	Azithromycin	Cold-fever, pneumonia, dental caries, tonsillitis, dysentery, diarrhea, typhoid fever, cough, sore throat, skin Infec, dyspareunia, postcoital bleeding, panic disorder, food poison, heartburn	15
	Erythromycin	Pneumonia, tonsillitis	2
3.	**Quinolones**		
	Ciprofloxacin	Appendicitis, fever, ear Infec, dysentery, diarrhea, cold-fever, buttock pain, Pneumonia, gonorrhea, heartburn, UTI, typhoid fever	12
	Levofloxacin	Cold-fever, eye Infec, asthma, cough	4
	Pepfloxacin	Typhoid fever, lung Infec	2
	Gatifloxacin	Cold-fever	1
	Sparfloxacin	Asthma	1
4.	**Penicillins**		
	Pen-V	Rheumatic fever	1
	Flucloxacillin	Injurious Infection, cough, lung abscesses, POI, throat Infec, fever, ear Infec, Sinusitis	8
	Amoxycillin	Cold-fever, diarrhea, influenza, nephrotic syndrome, POI, toothache	6
	Co-amoxyclub	Chronic headache, neck pain, stroke, throat Infec.	4
5.	**Tetracycline**	Cold-fever, cough, diarrhea, neck pain, urethritis	5
6.	**Others**		
	Cotrimoxazole	Cold-fever, headache	2
	Gentamycin	Conjunctivitis	1
	Chloramphenicol	Eye Infection	1
	Clindamycin	Toothache	1
	Rifampicin	Sided plural effusion/tuberculosis	1
	Metronidazole	Dysentery	1

[1]Frq: Frequency, [2]POI: post-operative Infection.

The usage pattern of different classes of antibiotics in the community

Mainly five groups of antibiotics, viz. cephalosporins, macrolide, penicillin, quinolone, tetracycline, were found to be prescribed. In cephalosporin group, 1GCs (cefazolin, cephalexin), 2GCs (cefuroxime), 3GCs (ceftriaxone, cefixime, ceftazidime) were found to be prescribed (Table 4) where the use of 3GCs was predominant but 4GCs and 5GCs were absent. In macrolide group, erythromycin and azithromycin were prescribed. In penicillin group, natural penicillin (Pen-V), β-lactamase resistant penicillin (flucloxacillin), aminopenicillin (amoxicillin, ampicillin) and penicillin/inhibitor combination (co-amoxiclub) were prescribed. In quinolone group, 2GQs (ciprofloxacin, pefloxacin) and 3GQs (levofloxacin, gatifloxacin, sparfloxacin) were prescribed but 4GQs were absent. In tetracycline group, short and long-acting tetracyclines were prescribed but intermediate acting tetracycline was absent. In other groups, sulfa drug, aminoglycoside, chloramphenicol, lincosamide, rifamycin, and metronidazole

were found to be prescribed. Notable point is that eleven β-lactum antibiotics (penicillins, cephalosporins) of cell wall synthesis-inhibitor have been extensively used, but DNA- and protein-synthesis inhibitors were used rarely. In our previous in vitro study, we showed that protein-synthesis inhibitors were satisfactorily effective against cephalosporin resistant uropathogen *Proteus* species (Chouduri and Wadud, 2014). Therefore, the rarely prescribed antibiotics can only be used as a weapon for the management of uncontrolled infection caused by resistant bacterial pathogens. This update, therefore, will help the physicians to choose an antibiotic for the treatment of infectious diseases.

Table 4: Antibiotics sold to consumers at retail pharmacies.

Cephalosporins	Macrolides	Penicillins	Quinolones	Tetracyclines	Others
Cefazolin	Erythromycin	Pen-V	Ciprofloxacin	Tetracycline	Cotrimoxazole
Cefrtiaxone	Azithromycin	Flucloxacillin	Levofloxacin	Doxycycline	Gentamycin
Cefalexin		Amoxycillin	Gatifloxacin		Chloramphenicol
Cefuroxime		Ampicillin	Pefloxacin		Clindamycin
Cefixime		Co-amoxiclub	Sparfloxacin		Rifampicin
Ceftazidime					Metronidazole

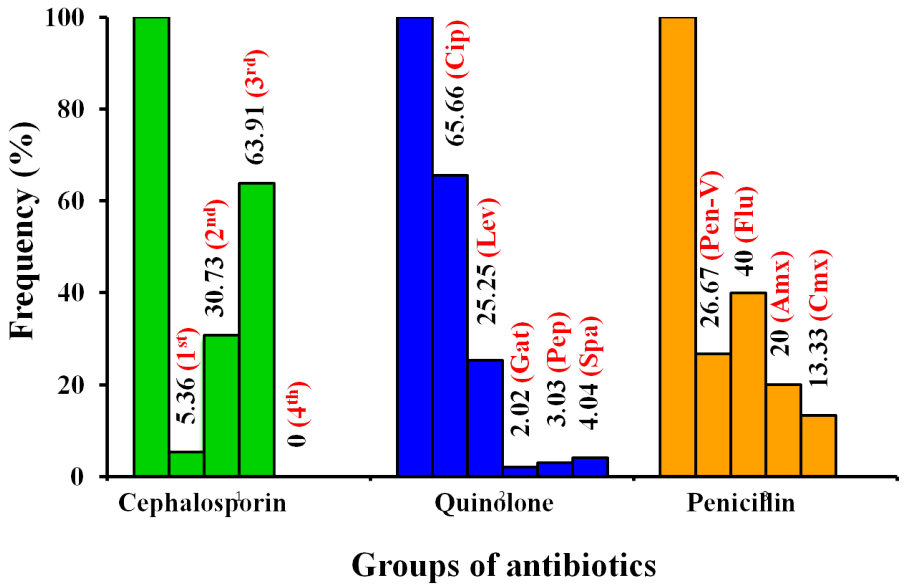

Fig. 1: Usage profile of three groups of antibiotics. 1st, 2nd, 3rd, 4th - respective generations of cephalosporin, Cip - ciprofloxacin, Lev - levofloxacin, Gat - gatifloxacin, Pep - pepfloxacin, Spa - sparfloxacin, PenV - penicillin V, Flu - flucloxacillin, Amx - amoxicillin, Cmx - co-amoxiclub. 3rd generation cephalosporin, ciprofloxacin, and flucloxacillin are maximally prescribed antibiotics in their respective groups.

Table 5: Frequency of suggested antibiotics in groups.

Groups of antibiotic	TSP	TAP (%)	FA-TAP (%)	FA-TSP (%)	Max
Cephalosporins	1100	598 (54.36)	205 (34.28)	205 (18.64)	3rd generation
Macrolides			78 (13.04)	78 (7.09)	Azitromycin
Quinolones			99 (16.55)	99 (9.00)	Ciprofloxacin
Penicillins			45 (7.52)	45 (4.09)	Flucloxacillin
Tetracyclines			28 (4.68)	28 (2.54)	
Metronidazoles			95 (15.88)	95 (8.64)	
Antifungals			24 (4.01)	24 (2.18)	
Others			24 (4.01)	24 (2.18)	

TSP: Total survey prescriptions, TAP: Total antibiotic suggested prescriptions, FA-TAP: Frequency of antibiotics out of TAP (n = 598), FA-TSP: Frequency of antibiotics out of the TSP (n = 1100), Max: Maximally prescribed antibiotics in their respective group.

Antibiotic group and prescribing trends

54.36% of prescriptions contained antibiotics (Table 5) indicating that the majority of patients had infections with/without other diseases. Group-wise list of prescribed antibiotics has been shown in table 5. Drugs of cephalosporin group were commonly prescribed (18.64% of total survey prescriptions [TSP] and 34.28% of total antibiotic suggesting prescriptions [TAP]) followed by that of quinolone group (9% of TSP, 16.55% of TAP), metronidazole (8.64% of TSP, 15.88% of TAP), macrolides (7.09% of TSP, 13.04% of TAP), and others (2–4% of TSP, 4–8% of TAP). It is likely that pathogens in the study area should be more opportunistic to develop resistance to cephalosporins. Strong cephalosporin resistance in genital pathogen *Neisseria gonorrhea* and uropathogen *Proteus* have already been documented in our previous reports (Chouduri and Wadud, 2013; Nesa *et al.*, 2013). Here 3GCs, azithromycin, ciprofloxacin, and flucloxacillin were maximally prescribed antibiotics in their respective groups.

A usage profile of individual antibiotic

The frequency of occurrence of each antibiotic in three groups, viz. Cephalosporin, quinolone, and penicillin was plotted to analyze the usage pattern of an antibiotic in their respective group (Figure 1). 3GCs were highly prescribed antibiotics (63.91%) in its group followed by 1GCs (5.36%) and 2GCs (30.73%). In quinolone group, ciprofloxacin was a highly prescribed drug (65.66%) followed by levofloxacin (25.25%), sparfloxacin (4.04%), pefloxacin (3.03%) and gatifloxacin (2.02%). In the penicillin group which is generally neglected as a backdated antibiotic in third world countries, especially in Bangladesh, flucloxacillin (40%) was widely prescribed antibiotic in this group. Other antibiotics, Pen-v, flucloxacillin, amoxicillin, and co-amoxiclav, were used apparently to a lower extent (13–27%).

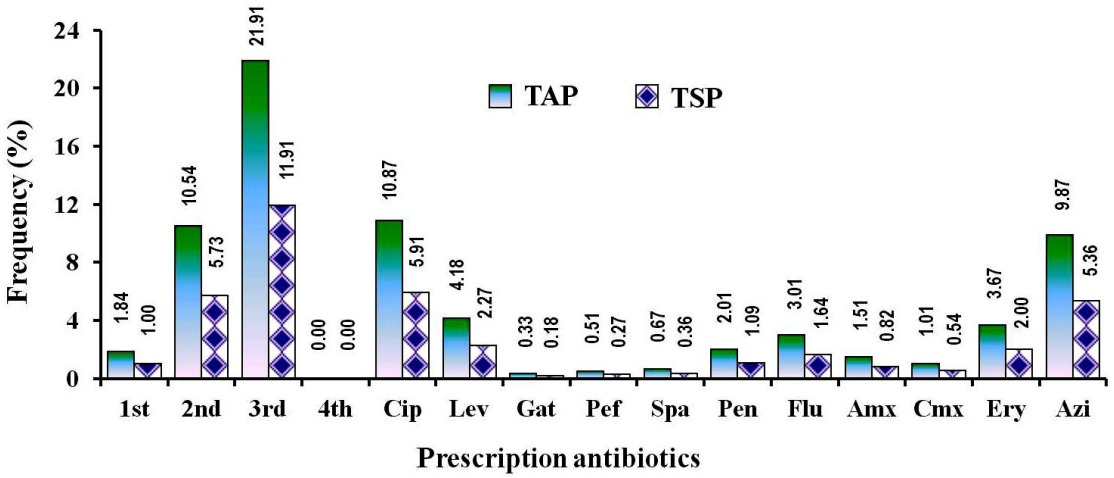

Fig. 2: Individual antibiotic in prescriptions. TAP: Total antibiotic containing prescriptions (n = 598), TSP: Total survey prescriptions (n = 1100). 1st, 2nd, 3rd, 4th - cephalosporins of their respective generations, Cip- ciprofloxacin, Lev- levofloxacin, Gat- gatifloxacin, Pef- pefloxacin, Spa- sparfloxacin, Pen- penicillin V, Flu- flucloxacillin, Amx- Amoxacillin, Cmx- co-amoxiclub, Ery- erythromycin, Azi- azithromycin.

Third generation cephalosporins (3GCs): Highly used antibiotics

The frequency of occurrence of each antibiotic with respect to the total survey prescriptions (TSP) and total antibiotic containing prescriptions (TAP) was compared (Figure 2). It was observed that among other antibiotics, 3GCs accounted for 11.91% of TSP and 21.91% of TAP. The highly prescribed 3GCs were ceftriaxone, cefixime, ceftazidime (Table 4). This result here probably explains why these antibiotics showed abnormally high resistances in our previous study (Chouduri and Wadud, 2014; Nesa *et al.*, 2013). The second highest prescribed antibiotic was ciprofloxacin (5.91% of TSP, 10.87% of TAP) followed by 2GCs (5.73% of TSP, 10.54% of TAP) and azithromycin (5.36% of TSP, 9.87% of TAP). Levofloxacin, erythromycin, and flucloxacillin accounted for more than 2% of TSP and 3% of TAP. The least prescribed antibiotics were 1GCs, penicillins, amoxicillin, co-amoxiclav, gatifloxacin, pefloxacin and sparfloxacin.

DISCUSSION

In this study, types of dosage forms of prescribed antibiotics were found to be missed in 17% of cases. In the majority of cases (73%), doctors prescribed antibiotics without any diagnostic tests and in 40% of cases, the complete directions for the use of antibiotic were absent. The missing of dosage forms in prescription may lead substandard dose during application of the antibiotics by the patients. No diagnosis and incomplete direction of the use of an antibiotic may produce unspecific target to pathogens and result in the incomplete inhibition of pathogens, respectively. These prescription errors are the initiators of the resistance property in pathogens. Moreover, the disease recovery among the patients was very low (12%) and in some cases (6%) prescribed antibiotics did not comply with the patients. Furthermore, a large number of patients (81%) had no comments about disease recovery, which indicated that patients were either bearing resistant pathogens or the prescribed antibiotics were unspecific to the pathogens. Nonetheless, 10% of patients were ordered by a combined therapy of antibiotics (Table 2) which favor our above speculation and indirectly revealed the existence of antibiotic resistance or recurrent/superinfections in patients. Therefore, omissions and errors in the prescription are the primary reasons for the triggering of resistance in pathogens. One of our recent reports (Haque *et al.*, 2016) described various prescription errors and omissions in Bangladesh.

In the present study, drugs of cephalosporin group specifically 3GCs were found to be extensively prescribed (Table 5, Figure 1). In Bangladesh, 3GC resistance was first reported in *Shigella* isolates in Dhaka during 2001–2002 and that time the increased MIC of ciprofloxacin was documented in the same report (Rahman *et al.*, 2004). Afterward, in 2013 we reported that *Neisseria gonorrhea* isolated from sex workers were ciprofloxacin resistant (Nesa *et al.*, 2013) but in another study, we showed ciprofloxacin sensitivity to uropathogen *Proteus* isolated from municipally supplied water (Chouduri and Wadud, 2014). In 2015, *Salmonella* was shown to be resistant to ampicillin, chloramphenicol, co-trimoxazole isolated from the patients of young children (30–39%) to adults (13%). In the same study, *Salmonella* isolates showed reduced susceptibility to ciprofloxacin and complete susceptibility to 3GCs and azithromycin (Khanam *et*

al., 2015). Therefore, the choice of antibiotics for the treatment of serious bacterial infections is rapidly changing. This is occurred by horizontal transfer of plasmid carrying antibiotic resistance. Such transfer of plasmid carrying 3GC resistance has been reported in Bangladesh in *E. coli* and *S. sonnei* strains collected from fecal specimens (Rashid and Rahman, 2014). However, the resistance of pathogens to antibiotics has been increasing for reasons related to the misuse of antibiotics.

Here, we showed the drugs of cephalosporin group were commonly prescribed (18.64% of total prescriptions and 34.28% of antibiotic-containing prescriptions) followed by that of the quinolone group (9% of total prescriptions and 16.55% of antibiotic-containing prescriptions). 3GCs (63.91%) and ciprofloxacin (65.66%) were highly prescribed antibiotics in their respective group (Figure 1). Notable point is that β-lactum antibiotics (penicillins, cephalosporins) of cell wall synthesis-inhibitor were used extensively, but DNA- and protein-synthesis inhibitors were used rarely. We showed backdated or rarely used antibiotics were satisfactorily effective against pathogens *in vitro* than that of the cell wall- and folate-synthesis inhibitors (Chouduri and Wadud, 2014). The repeated use of a distinct group of antibiotics may generate the reduced susceptibility and ultimately resistance to pathogens. On the other hand, visiting quack doctors might be the cause of the increased chance of irrational use and unethical dose regimen of antibiotics leading to the development of drug resistance, recurrent infection, superinfections and ultimately uncontrolled disease management. Based on the diseases enlisted in table 3, relatively a high frequency of postoperative infection (POI) was found assuming that either the patients were not conscious about the proper use of antibiotics at the postoperative stage or the suggested antibiotics were therapeutically ineffective due to the development of antibiotic resistance in pathogens. Therefore, prescribers need to be more professional to the use of antibiotics and the users should follow the guidance ordered by the prescribers.

We searched the usage patterns of antibiotics and their inhibitory effects on pathogens in neighboring countries, Nepal, India, and Pakistan, to compare the profile presented in this study. Ampicillin, ampicillin in combination with cloxacillin, aztreonam were resistant to *Klebsiella oxytoca* strain, the single and combination of antibiotics were found to be prescribed in Nepal (Shrestha *et al.*, 2012). Very recently, a study conducted on blood cultures for *Salmonella enterica* suggested that fluoroquinolones should not be used for the treatment of enteric fever in Nepal (Arjyal *et al.*, 2016). Cephalosporin usage is highest in urban hospitals and pharmacy shops in India than rural hospitals (Chandy *et al.*, 2013). A survey conducted in South India showed that among 52,788 outpatients about 40.9% were prescribed with antibiotics (Chandy *et al.*, 2013) but here in Bangladesh in this study 54.36% of outpatients were ordered with antibiotics (Table 1) which is significantly higher than India. Fluoroquinolones and penicillins were widely used antibiotics in South India and cephalosporins were more often used in urban private hospitals (Chandy *et al.*, 2013). Another survey conducted on outpatients in Nepal had shown that 46.1% patients were male and 53.9% female (Lamichhane *et al.*, 2006). In our study, the case of infections in male outpatients (67%) was higher than that of female (32%) which was rationally expected because the male people have to be outdoor more for works, family issues, and social needs. Among patients who were suggested antibiotics 50.50% of them were in the age group of 16–30 years (Table 1). The same reasons mentioned above are plausible for the patients of age 16–30 years since they are young and have to be outdoors. In Nepal, the highest number of patients (28.9%) were in the age group 15–25 years. Commonly prescribed group of drugs were antibiotics (16.5%) among the total prescribed drugs. Penicillins were the most commonly prescribed antibiotics (36.6%) followed by quinolones (19.6%) (Lamichhane *et al.*, 2006). Carbapenems generally used for the treatment of infections caused by multi-drug resistant pathogens are very recently found to be resistant in Pakistan (Anwar *et al.*, 2016).

CONCLUSIONS

Countrywide educational campaigns on rational use of antibiotic are urgently needed although the findings obtained cannot be generalized to the whole population of Bangladesh. Establishing a drug regulatory authority is critical to improve the quality use of antibiotics. Moreover, physicians prescribing habits should not be biased to a particular antibiotic and/or pharmaceutical company.

ABBREVIATIONS

MBBS: Bachelor of medicine and bachelor of surgery; BDS: Bachelor of dental surgery; NSAIDs: Nonsteroidal anti-inflammatory drugs; WMA: World medical association; TSP: Total survey prescriptions; TAP: Total antibiotic containing prescriptions; 1GCs/2GCs/3GCs: First/second/third generation cephalosporins.

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AUTHORS CONTRIBUTION

MB prepared the questionnaire and coordinated in the survey procedure; MUH, SIA, NU, NK, RA, AH contributed to data collection; AUC analyzed data and drafted the manuscript. All authors contributed to the study conception and design.

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COMPETING INTERESTS

The authors declared no competing interests.

ETHICS APPROVAL

This study was approved by a University Ethics Committee formed in Institute of Biological Sciences.

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