



বঙ্গবন্ধু শেখ মুজিব মেডিক্যাল বিশ্ববিদ্যালয়  
Bangabandhu Sheikh Mujib Medical University

# Antimicrobial Guideline

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**Dynamic online antimicrobial guideline with stewardship program: Impact on antimicrobial prescribing**

## Dynamic online antimicrobial guideline with stewardship program: Impact on antimicrobial prescribing

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### Abstract

Dynamic online antimicrobial guideline with stewardship program was attempted in Bangabandhu Sheikh Mujib Medical University (BSMMU) to improve the antimicrobial prescribing. The prescribing pattern was evaluated by retrospective prescription audit. Overall 59.4% of admitted patients of four selected departments received antimicrobials. Highest (81.9%) was in the Department of Obstetrics and Gynecology, followed by Surgery (78.5%), Internal Medicine (47.6%) and Pediatrics (46.7%). After launching of guideline, antimicrobial prescribing was significantly reduced in the Department of Internal Medicine (47.6% to 22.2%;  $p < 0.01$ ) and Pediatrics (50.0% to 40.0%;  $p < 0.01$ ). Significant ( $p < 0.05$  to  $p < 0.001$ ) change was observed with different antimicrobials in different departments. Consumption of cefixime ( $8.5 \pm 3.7$  to  $3.9 \pm 2.5$ ;  $p < 0.05$ ) and ceftriaxone ( $6.9 \pm 3.4$  to  $3.1 \pm 2.2$ ;  $p < 0.005$ ) was reduced significantly in Internal Medicine. The adherence to guideline was highest in the Department of Obstetrics and Gynecology (91.3%) followed by Pediatrics (86.3%) and Internal Medicine (81.2%).

### Introduction

Bangladesh is going through a transition in health (WHO, 2015), however the major causes of morbidity and mortality are still infective diseases and therefore antimicrobials are the most widely used medicine (Rahman and Huda, 2014; WHO, 2015; DGHS, 2016). Prescribing of antimicrobials in Bangladesh is generally irrational (Guyon et al., 1994; Rahman et al., 1998; Baqui et al., 1999; Islam et al., 2007; Afreen and Rahman, 2014).

Guidelines are considered as reflection of collective wisdom and antimicrobial guideline is effective to contain irrational prescribing of antimicrobials (Farrar, 1985; Sanson-Fisher et al., 1993; Hogerzeil, 1995; Finch, 1998). Bangabandhu Sheikh Mujib Medical University (BSMMU) antibiotic guidelines 2005 was the first institutional guideline in Bangladesh on use of antimicrobials (BSMMU, 2005), though adherence to

that guideline was not satisfactory (Siddika, 2012).

Antimicrobial stewardship program (ASP) is considered as the most effective approach to improve antimicrobial prescribing (Carling et al., 2003; MacDougall and Polk, 2005; Lee et al., 2013; Barlam et al., 2016; CDC 2016). ASP encourage clinician to improve quality of care through better infection cure rate (Schiff et al., 2001; Owens et al., 2004; Abbo et al., 2011). On this backdrop, ASP was designed in BSMMU to support the implementation of updated antimicrobial guideline. The experience and evaluation of this guideline would provide important information for the researcher community and policy makers working on antimicrobial resistance and its containment.

### Materials and Methods

The 'Formative Research' was conducted as a before-



after study in BSMMU Hospital from April 2015 to February 2016, and the impact was evaluated in the selected departments, e.g., Departments of Internal Medicine, Obstetrics & Gynecology, Pediatrics and Surgery. Before initiating the actual study, ethical clearance was obtained from the Institutional Review Board of BSMMU.

Initially, the existing situation was analyzed by retrospective review of 600 antimicrobial containing prescriptions of the admitted patients stored in the record room. For situation analysis, antimicrobial prescribing pattern was assessed by proportion of prescription containing antimicrobial. Sensitivity pattern of the cultured microbes in the Department of Microbiology of BSMMU during 2013 and 2014 were collected, compiled and analyzed.

After collection of information for situation analysis, Questionnaire survey and Focus Group Discussions (FGDs) were conducted among the key stakeholders and prescribers to get insight, opinion and feedback regarding features, format and methodology of updating and formulation of guideline as well as components of the ASP for BSMMU.

For evaluation of intervention, 30 inpatients prescriptions containing antimicrobials were collected from each studied department just immediately before and after intervention. These prescriptions were then reviewed, compiled and analyzed (WHO, 2003). Change in the overall antimicrobial prescribing was evaluated by comparing proportion of prescription

containing antimicrobial, Defined Daily Dose (DDD) per 100 bed days of commonly prescribed antimicrobial and DDD consumed per admitted patient received antimicrobials before and after intervention. Change in prescribing of every antimicrobial was evaluated separately. The coverage of the guideline was evaluated by the proportion of mentioned diagnosis of the treatment sheet present in the guideline. The adherence to the guideline was later evaluated only in the departments in which guideline covered more than 50% of diagnoses mentioned in the treatment sheets. Guideline adherence was evaluated by the consistency of prescribed antimicrobial in the treatment sheet with the mentioned antimicrobial for that particular diagnosis.

#### **Description of the intervention**

*Formulation of antimicrobial guideline:* The results of situation analysis were provided to the members of the committee authorized to update and formulate BSMMU antibiotic guideline. Then the methodology of guideline formulation was adopted in the meeting. After that, a draft template to collect opinion was formulated considering local context and global norms, which was sent to all chairpersons. On the basis of the preferences and recommendations, a draft antimicrobial guideline was prepared by the committee and sent to the prescribers for feedback. After endorsement, the Antimicrobial guideline was finalized, online version of which was launched on 14th December 2015 in presence of highest administration of the University.

*Antimicrobial stewardship program (ASP):* Antimicrobial

#### **Box 1: Procedure of the study**

##### **Situation analysis**

Antimicrobial prescribing data collection for situation analysis



Microbial sensitivity pattern of the common microbes of 2013 and 2014 were collected



Compilation of the results for situation analysis



##### **Awareness building towards development of consensus about methodology among the Committee members**

Provision of the result to the members of committee authorized to develop/update antibiotic guideline



Adoption of methodology for updating and formulation of antimicrobial guideline



##### **Sensitization, awareness building and opinion collection from the key prescribers**

Dissemination of the result to the chairpersons of all departments



Collection of opinion of the prescribers of different departments about their preference of antimicrobials in common condition



Series of interactive meetings with the stakeholders, i.e., key prescribers



##### **Formulation of the antimicrobial guideline**

Formulation and circulation of first draft of antimicrobial guideline for feedback



Finalization of the online version of antimicrobial guideline



##### **Antimicrobial stewardship program for implementation of guideline**

Launching of online version of the antimicrobial guideline of BSMMU



Reminders about antimicrobial guideline through SMS to all prescribers



Academic detailing by the investigator to provide relevant scientific evidences to the key prescribers in order to explain the benefits of adhering the antimicrobial guideline



Assessment of the impact of intervention by comparing antimicrobial prescribing data immediately before and after launching of antimicrobial guideline

Stewardship was executed by active participation of the key prescribers during the process of development of guideline as well as the formal commitment, endorsement and persuasion from of the top level management of the University.

*Reminders:* Repeated reminders were sent to the key prescribers and other stakeholders through SMS by the investigators on behalf of the committee authorized for the purpose.

*Academic detailing:* Face-to-face educational visits conducted by the investigator along with provision of scientific evidences to the prescribers.

#### Post-intervention data collection

Data was collected immediately before and after 15 days of introducing the antimicrobial guideline 2015 to evaluate the impact of intervention.

#### Statistical analysis

Data was compiled, presented and appropriate statistical test was applied (paired proportion test and unpaired t-test) to draw the expected conclusion. Microsoft Excel 2007 was used for the statistical analysis. P value was calculated by test statistic (t value) using online calculator against corresponding degree of freedom (df).

## Results

Table I revealed that among the admitted patients, overall 59.4% received antimicrobial in BSMMU hospital. Of those, highest antimicrobials were prescribed in the Department of Obstetrics & Gynecology (82.0%) followed by the Departments of Surgery (78.5%), Internal Medicine (47.6%) and Pediatrics (46.7%).

The questionnaire survey revealed that half of the prescribers are unaware about existence of BSMMU antimicrobial guideline 2005 and none ever followed that. Different managerial and scientific issues were raised and mentioned. Moreover, measures were suggested by the respondents for successful implementation of newly formulated guideline (detail in the supplementary file).

After introduction of the updated dynamic online guideline along with implementation of ASP, proportion of patient received antimicrobial significantly reduced from 47.6% to 22.2% ( $p < 0.01$ ) and 50% to 40% ( $p < 0.05$ ) respectively in the departments of Internal Medicine and Pediatrics. No statistically significant change was observed in the departments of Obstetrics and Gynecology, and Surgery (Table II).

Change was observed after intervention in the pattern of antimicrobial prescribing (DDD/100 bed days),

**Table I**

#### Proportion of admitted patients received antimicrobials

Department	Proportion of patients received antimicrobial
Internal Medicine	47.6% (150/315)
Surgery	82.0% (150/183)
Obstetrics and Gynecology	46.7% (150/321)
Pediatrics	78.5% (150/191)
Total	59.4% (600/1010)

Percentage = Total number of prescriptions (150) contained antimicrobial/total number of prescriptions reviewed to obtain those prescriptions

**Table II**

#### Effect of intervention on proportion of antimicrobial use

Department	Proportion of patients received antimicrobial		
	Immediately before intervention (n=63)	Immediately after intervention (n=135)	p value
Internal Medicine	47.6% (30/63)	22.2% (30/135)	<0.01
Surgery	81.0% (30/37)	85.7% (30/35)	
Obstetrics & Gynecology	90.9% (30/33)	85.7% (30/35)	
Pediatrics	50.0% (30/60)	40.0% (30/75)	<0.01

Paired proportion test was done;  $p < 0.05$  was considered as statistically significant; Immediately before intervention: prescribing data of the most recent patients, i.e., immediately before launching of the guideline; Immediately after intervention: prescribing data of the most recent patients, i.e., immediately after launching of the guideline

which was statistically significant ( $p < 0.05$ ) in case of few antimicrobials in different departments (Table III).

Table IV shows that after intervention, in the department of Internal Medicine, consumption (total DDD consumed per patient as expressed in mean  $\pm$  SD) of cefixime ( $8.5 \pm 3.7$  to  $3.9 \pm 2.5$ ;  $p < 0.05$ ) and ceftriaxone ( $6.9 \pm 3.4$  to  $3.1 \pm 2.2$ ;  $p < 0.005$ ) was reduced significantly. In addition, antimicrobial prescribing was changed in other departments, though that change was not reflected significantly at the level of individual antimicrobial.

Table V shows the coverage of diagnoses in the BSMMU antimicrobial guideline 2015 was highest (76.7%) in Department of Obstetrics and Gynecology followed by departments of Pediatrics (73.3%) and Internal Medicine (53.3%). The adherence with the guideline was highest in Department of Obstetrics and

Table III						
Effect of anti-microbial guideline with ASP on overall use of antimicrobials (expressed in DDD/100 bed days)						
Name of the departments	Name of antimicrobials	ATC codes	Immediately before intervention (DDD/100 bed days)	Immediately after intervention (DDD/100 bed days)	Test statistic	p value
Internal Medicine	Cefixime	J01DD08	n = 63 6.3	n = 135 6.7	0.1	<0.05
	Ceftriaxone	J01DD04	17.5	7.4	2.0	
	Cefuroxime	J01DC02	6.3	1.5	1.7	
	Co-amoxiclav	J01CR02	9.5	3.7	1.6	
	Metronidazole	J01XD01	3.2	1.5	0.8	
Obstetrics and Gynecology	Cefixime	J01DD08	n = 33 9.1	n = 35 5.7	0.9	<0.001
	Ceftriaxone	J01DD04	63.6	77.1	1.1	
	Cefuroxime	J01DC02	27.3	5.7	3.8	
	Metronidazole	J01XD01	100.0	57.1	3.4	
Pediatrics	Ceftriaxone	J01DD04	n = 60 26.7	n = 75 10.7	2.6	<0.01
	Cefuroxime	J01DC02	5.0	4.0	0.3	
	Ciprofloxacin	J01MA02	18.3	12.0	1.2	
	Flucloxacillin	J01CF05	15.0	1.3	3.4	
Surgery	Amikacin	J01GB06	n = 37 5.4	n = 35 2.9	0.9	<0.05
	Cefixime	J01DD08	27.0	25.7	0.2	
	Ceftriaxone	J01DD04	27.0	45.7	2.2	
	Cefuroxime	J01DC02	32.4	45.7	1.5	
	Metronidazole	J01XD01	18.9	25.7	1.0	

p≤0.05 was considered as statistically significant with a test statistic value more than 1.96

Table IV								
Effect of antimicrobial guideline with ASP on use of individual antimicrobials (expressed in total DDD consumed per admitted patient who received antimicrobials)								
Name of the departments	Name of antimicrobials	ATC codes	n	Immediately before intervention	n	Immediately after intervention	Test statistic	p value
Internal Medicine	Cefixime	J01DD08	4	8.5 ± 3.7	9	3.9 ± 2.5	2.3	<0.05
	Ceftriaxone	J01DD04	11	6.9 ± 3.4	10	3.1 ± 2.2	3.2	<0.005
	Cefuroxime	J01DC02	4	10.6 ± 6.9	2	12.0 ± 0.0	0.4	
	Co-amoxiclav	J01CR02	6	9.7 ± 4.7	5	13.1 ± 0.0	1.8	
	Metronidazole	J01XD01	2	4.7 ± 3.5	2	3.0 ± 4.2	0.4	
Obstetrics and Gynecology	Cefixime	J01DD08	3	4.2 ± 0.3	2	6.8 ± 3.2	1.2	
	Ceftriaxone	J01DD04	21	2.9 ± 1.6	27	3.3 ± 3.6	0.5	
	Cefuroxime	J01DC02	9	2.9 ± 1.3	2	1.0 ± 1.4	1.7	
	Metronidazole	J01XD01	33	3.7 ± 2.6	20	5.1 ± 5.1	1.2	
Pediatrics	Ceftriaxone	J01DD04	16	4.6 ± 6.5	8	6.0 ± 5.1	0.6	
	Cefuroxime	J01DC02	3	14.1 ± 5.4	3	16.8 ± 17.5	0.3	
	Ciprofloxacin	J01MA02	11	2.4 ± 0.8	9	2.3 ± 0.8	0.3	
	Flucloxacillin	J01CF05	9	2.7 ± 2.0	1	3.0 ± 0.0	0.5	
Surgery	Amikacin	J01GB06	2	6.3 ± 1.8	1	4.3 ± 0.0	1.6	
	Cefixime	J01DD08	10	3.3 ± 3.2	9	3.9 ± 3.3	0.4	
	Ceftriaxone	J01DD04	10	3.3 ± 2.4	16	3.1 ± 1.8	0.2	
	Cefuroxime	J01DC02	12	3.8 ± 3.0	16	2.8 ± 1.9	1.0	
	Metronidazole	J01XD01	7	3.4 ± 2.5	9	2.3 ± 1.6	1.0	

Unpaired t test was done; p≤0.05 was considered as statistically significant; SD = Standard Deviation

**Table V****Proportion of diseases mentioned in BSMMU antimicrobial guideline 2015 and rate of guideline adherence**

Name of the departments	Coverage in BSMMU antimicrobial guideline 2015	Adherence
Internal Medicine	53.3% (16/30)	81.2% (13/16)
Obstetrics & Gynecology	76.7% (23/30)	91.3% (21/23)
Pediatrics	73.3% (22/30)	86.3% (19/22)

Coverage means proportion of diagnosis mentioned in the treatment sheet present in the guideline; Adherence means proportion of prescription, selection of which adhered/matched to the antimicrobial mentioned in BSMMU antimicrobial guideline 2015 for that diagnosis

Gynecology (91.3%) followed by departments of Pediatrics (86.3%) and Internal Medicine (81.2%). Post intervention adherence data of the Department of Surgery was not presented as very few (less than 50%) of the diagnoses mentioned in treatment sheets were present in the guideline.

## Discussion

Present study revealed that overall 59.4% of admitted patients received antimicrobial, of which, highest (81.9%) in the department of Obstetrics and Gynecology, followed by Surgery (78.5%), Internal Medicine (47.0%) and Pediatrics (46.7%). These findings correspond with the result of studies conducted in the similar hospital (Siddika, 2012; Shah et al., 2016).

The qualitative part of the study showed that almost everybody has forgotten about the antimicrobial guideline of 2005. Active participation of the key prescriber, utilization of culture sensitivity reports of the hospital samples, availability of online, offline and hard copy of the guideline, regular updating and motivational programs were suggested by the key prescribers. These suggestions were analogous to the recommendations of different previous studies and reports (Skodvin et al., 2015; NSCARB, 2014; NAP, 2016).

Significant reduction ( $p < 0.01$ ) in antimicrobial prescribing was observed in the departments of Internal Medicine and Pediatrics, which did not happen in other two departments. The reduction of antimicrobial prescribing had been mentioned earlier in a meta-analysis involving 30 high quality researches (Davey et al., 2013). However, the findings of other two departments are not possible to explain through the present study, as that requires further in-depth exploration.

The coverage of diagnoses mentioned in treatment sheets in the guideline was more than 50 percent in

three departments (departments of Internal Medicine, Obstetrics and Gynecology, and Pediatrics). The reason of low coverage of the guideline needs to be identified through detail exploration and long-term collaboration with key prescribers of different department with special emphasis on surgeons as their coverage was very low.

The adherence to guideline was more than 80 percent in three departments (Internal Medicine, Obstetrics and Gynecology, and Pediatrics). Similar rate of adherence to guidelines was observed in a number of previous studies (Abbo et al., 2011; Chandy et al, 2014; Alweis et al., 2014). Adherence to guideline could not be measured in the department of Surgery as very few diagnoses mentioned in the treatment sheet were present in the antimicrobial guideline.

The present study attempted to establish a new platform, which incorporated an online version of antimicrobial guideline that is upgradable easily by the user of certain authority, which can receive feedback and generate message to all about the feedback in order to sensitize every prescriber on that issue, can generate reminders on regular intervals, can generate report to be disseminated among targeted users. On the top of everything, this type of intervention requires least resource. Very limited experience about such approach is available till now (Haffey et al., 2013). Some of the famous hospitals of the world have different types of guidelines (JHHASP, 2015, Cleveland Clinic, 2012, MHM, 2008), though the approach attempted in the present study is an innovative one.

Considering the above findings, method of formulation, introduction and upgrading of antimicrobial guideline 2015 may be considered as a model intervention. Success of this ongoing ASP in the apical medical institution of Bangladesh might be an example of application of Information Technology to encounter the challenge of antimicrobial resistance in developing and least developed countries. Findings of the present study revealed that a comprehensive approach can bring a positive change in antimicrobial utilization.

## Conclusion

A dynamic online platform for ASP including antimicrobial guideline might be an option for policy makers to incorporate or implement in Bangladesh in order to improve antimicrobial prescribing in teaching hospital.

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## Conflict of Interest

Authors declare no conflict of interest

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**Supplementary Table I**

**Key prescribers knowledge and perception about BSMMU antimicrobial guideline 2005**

*Knowledge and perception*

Half of the prescribers did not know that BSMMU has an antibiotic guideline since 2005

More than half of the prescribers have not seen the antibiotic guideline of BSMMU 2005

None of them followed recommendations of the guideline during their prescribing

Half of them depend on their experience during antimicrobial prescribing empirically need of the situation

Most of them have no regular access to the sensitivity report of BSMMU

**Supplementary Table II**

**Key prescribers suggestions about BSMMU antimicrobial guideline 2015**

*Suggestions on managerial issues*

The prescribers should be motivated

Active participation of the key prescribers should be ensured

Guideline should have be available in different formats like, web-based version, printed version and downloadable mobile application

Guideline should reach the end user

*Suggestions on scientific issues*

Recommendations should be supported by the laboratory evidence and other relevant scientific documents

Guideline should be updated regularly on the basis of culture sensitivity reports

Contents should be arranged according to the systems in alphabetic order and then diseases under each system should be arranged alphabetically again

Prophylactic use of antimicrobial in surgery should be separately mentioned

Antimicrobials should be categorized in pregnancy category A, B, C

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