Drug utilization, rationality, and cost analysis of antimicrobial medicines in a tertiary care teaching hospital of Northern India: A prospective, observational study

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Abstract:
BACKGROUND: The burden of bacterial infections is huge and grossly under-represented in the current health-care system. Inappropriate use of antimicrobial medicines (AMMs) poses a potential hazard to patients by causing antibiotic resistance. This study was conducted to assess the: (i) AMM consumption and use patterns in patients attending the outpatients and inpatients of Medicine and Surgery departments of the hospital. (ii) Appropriateness of the AMM in the treatment prescribed, and (iii) cost incurred on their use in admitted patients.

MATERIALS AND METHODS: An observational, prospective study was conducted among inpatients and outpatients of the Medicine and Surgery departments of a tertiary care hospital of northern India. Analysis of 2128 prescriptions and 200 inpatient records was performed using a predesigned format. The use of AMMs was reviewed using anatomical therapeutic chemical classification and defined daily doses (DDDs). To evaluate the expenditure incurred on AMMs, ABC analysis was performed.

RESULTS: AMMs were prescribed to 37.9% outpatients and 73% of admitted patients. The percentage encounters with AMMs was 40.6% (medicine) and 25.6% (surgery) outpatients. The total DDDs/100 patient days of AMMs in medicine and surgery were 3369 and 2247. Bacteriological evidence of infection and AMM sensitivity was present in only 8.5% of cases. Over 90% of AMMs were prescribed from the hospital essential medicines list. Most of the AMMs were administered parenterally (64.9%). Multiple AMMs were prescribed more to inpatients (84.2% vs. 4.2% outpatients). Overall, expenditure on AMM was 33% of the total cost of treatment on medicine. ABC analysis showed that 74% of the expenditure was due to newer, expensive AMM, which constituted only 9% of the AMM used. The AMM therapy was found to be appropriate in 88% of cases as per Kunin's criteria for rationality.

CONCLUSION: AMMs are being commonly prescribed without confirmation of AMM sensitivity in the hospital. A large proportion of expenditure is being incurred on expensive AMM used in a few number of patients. There is a need for developing a policy for rational use of AMM in the health facility.

Keywords: Antimicrobials, drug utilization, expenditure, prescription pattern, rationality

Introduction

Inappropriate use of antimicrobial medicines (AMMs) is an issue of global concern as it directly contributes to the development of antimicrobial resistance (AMR) and increased health-care costs. As much as 15%–30% of the health budget is attributed to AMR worldwide.[1]
The problems due to irrational use of AMMs are amplified in developing countries like India, wherein there is huge burden of infectious diseases.[2,4] Lack of prescribing guidelines and easy over the counter availability of them has led to their injudicious use.

Public health facilities in India are overburdened with a large number of patients. In such a scenario, patients are often prescribed medicines including AMM without confirmation of diagnoses, as the laboratories may not have the capacity to determine the AMM sensitivity of biological samples.[7]

One of the strategies to curtail AMR and promote rational use of AMMs is to frame local AMM policies. For formulation and monitoring of such policies, data on AMM utilization patterns are crucial. Unfortunately, data on AMM utilization are frequently unavailable.[8]

Lok Nayak Hospital is a public health, tertiary care, teaching hospital, in Delhi (India) with 1676 beds. It caters to around 70,000 inpatients and 10 lakh outpatients annually.[9] As per Government policies, the hospital gives medicines free of cost to the patients. However, only medicines in the hospital essential medicine list (EML) are freely available.[10]

The current study aims at studying the prescription pattern, rationality of AMMs, expenditure incurred in patients of medicine and surgery departments and focuses on their prescribing trends.

**Materials and Methods**

The study was conducted in the Department of Pharmacology, Maulana Azad Medical College in collaboration with Departments of Medicine and Surgery, Lok Nayak Hospital, Delhi for 1 year after prior approval by the Institutional Ethics Committee (F.17/IEC/MAMC/12/No. 138).

**Study design**

The study design involves observational, cross-sectional in outpatients and observational, prospective in inpatients.

**Sample size**

It was decided based on the study conducted by National Cent for Containment of AMR, wherein 5% of the inpatient load was enrolled in the study.[11] Keeping practicality and feasibility in mind, 5% of annual inpatient load and 2.5% of outpatient load of one unit in each medicine and surgery was included in the study.

For outpatients, a total of 1512 and 606 new prescriptions were randomly analyzed in the medicine and surgery outpatient department, respectively. The prescription of every second patient exiting the outpatient department was reviewed.

In Inpatients a total of 200 case records each in medicine and surgery departments were randomly assessed. The records of patients who were prescribed one or more AMMs were separated from the total records of admitted patients and put in increasing order of the patient’s record number. Every third case record was reviewed for use of AMM. The treatment given to the patients was assessed on a daily basis till the patient was discharged. No interference with the patient’s hospital treatment was done.

A predesigned, structured pro forma was used for collecting data. The pro forma was divided into following sections; (i) patient demographic details, (ii) history of illness, (iii) treatment history, and (iv) AMM use characteristics which included signs and symptoms suggestive of infection and laboratory evidence of infection, indication for the use of AMM whether therapeutic or prophylactic, availability of antibiotic sensitivity data, AMM prescribed (generic name, dose, dosage form, and frequency). The inclusion of AMM in the EML was assessed.

The prescribed medicines were classified according to the International Anatomic therapeutic Chemical Classification System.[12] The extent of AMM utilized was quantified using defined daily doses (DDD) and DDDs per 100 patient days. The appropriateness of the AMM prescribed was assessed based on Kunin’s criteria.[13] This was based on an exhaustive clinical and medical literature review (Available Standard Treatment Guidelines in India, recommendations of National Health programs, World Health Organization, and Guidelines of National and International Professional bodies).[14-17]

The cost of all the medicines prescribed to the patients was calculated in Indian Rupees using the hospital medicine rate list (1 USD = 64.38 INR). For the medicines which were not mentioned in the hospital rate list, the cost was calculated as the average of market costs of different brands of the same medicine given in a medicines compendium “Drugs Today.”[18] ABC analysis of expenditure incurred on AMM was performed. The expenditure on AMM according to the route of administration and inclusion of AMM in the hospital EML was determined.

**Statistical analysis**

The data were entered in computer software MS Excel. Computer software SPSS, version 17.0 (Microsoft, Redmond, Washington, United States) was used for the analysis. The data have been expressed as mean ± standard
deviation (range). For continuous variables, unpaired Student’s t-test was used. The categorical variables were compared using Chi-square test. A value of $P < 0.05$ was considered statistically significant.

**Results**

The demographic characteristics of patients in medicine and surgery departments in both outpatients and inpatients were comparable. The duration of stay of patients in the hospital was longer ($P < 0.05$) in medicine department than in surgery department. Males were predominant in both departments [Table 1]. The ten most common conditions for which AMM were prescribed in medicine and surgery are shown in Table 2.

**Utilization pattern of antimicrobial medicines**

**Outpatients**

Overall the total numbers of medicines prescribed were 5976. On an average, 2.52 medicines were prescribed to a patient. The AMM prescription encounters and AMMs prescribed as a percentage of total medicines were higher in medicine compared to surgery ($P < 0.05$).

**Table 1: Demographic characteristics of patients in medicine and surgery outpatients and inpatients**

| Variable                      | Medicine | Surgery | Overall |
|-------------------------------|----------|---------|---------|
| **Outpatients**               |          |         |         |
| Age (years)                   | 52.1±14.9| 51.6±15.6| 52.5±15.1|
| Range                         | 12-91    | 13-88   | 12-91   |
| Gender, n (%)                 |          |         |         |
| Females                       | 709 (46.8)| 283 (45.9)| 992 (46.6)|
| Males                         | 803 (53.1)| 333 (54.0)| 1136 (53.3)|
| **Inpatients**                |          |         |         |
| Age (years), mean±SD          | 46.2±13.2| 38.6±15.6| 42.5±16.1|
| Range                         | 18-86    | 16-78   | 16-86   |
| Gender, n (%)                 |          |         |         |
| Females                       | 91 (45.5)| 78 (39)  | 169 (42.2)|
| Males                         | 109 (54.5)| 122 (61) | 231 (57.8)|
| Duration of stay in hospital  | 6.4 (1-21)*| 3.8 (1-16)| 5.1 (1-21)|

*P<0.05. SD=Standard deviation

**Table 2: Ten most common conditions for which antimicrobial medicine were prescribed**

| Medicine (n=200)          | n (%)* | Surgery (n=200)          | n (%)* |
|---------------------------|--------|--------------------------|--------|
| Pulmonary tuberculosis    | 49 (24.5)| Cholelithiasis         | 56 (28)|
| Pneumonia                 | 46 (23) | Hemia                 | 45 (22.5)|
| Lower respiratory tract infections other than pneumonia | 39 (19.5) | Acute appendicitis | 21 (10.5)|
| Liver cirrhosis           | 28 (14) | Carcinoma breast       | 18 (09)|
| Sepsis                    | 25 (12.5)| Renal calculus          | 12 (06)|
| Urinary tract infection   | 15 (7.5) | Intestinal perforation with peritonitis | 12 (06)|
| Bacterial meningitis      | 11 (5.5) | Traumatic injuries      | 11 (5.5)|
| Rheumatic heart disease   | 11 (5.5) | Appendicular abscess    | 9 (4.5)|
| Acute gastroenteritis     | 9 (4.5)  | Subacute intestinal obstruction | 9 (4.5)|
| Encephalitis              | 5 (2.5)  | Gangrene               | 3 (1.5)|

*The total percentage is >100, as some patients had multiple comorbidities

The prescriptions with multiple AMMs were also more in medicine department [Table 3].

The most common AMM prescribed overall in medicine and surgery departments were amoxicillin-clavulanate (32.1%), azithromycin (21.2%), metronidazole (14.1%), ciprofloxacin (8.1%), norfloxacin (3.3%), and nitrofurantoin (4%) [Figure 1].

Majority of the AMM were prescribed from the EML of Delhi (97.8%). The AMM prescribed outside the EML were amoxicillin + cloxacillin (7), cefixime (4), tinidazole + norfloxacin (3), ofloxacin (2), and tinidazole + ofloxacin (1), (the number in the bracket is the number of prescriptions). Four fixed dose combinations (FDC) of AMM were prescribed. They were amoxicillin + clavulanate (260), amoxicillin + cloxacillin (7), tinidazole + norfloxacin (3), tinidazole + ofloxacin (1).

**Inpatients**

A total of 4208 case sheets of inpatients in medicine and surgery department were reviewed, of which, 3105 (73.7%) had at least one AMM prescribed [Table 4], AMM constituted 40% of the total medicines prescribed. A total of 33 individual AMM were prescribed and the average number of AMM used per patient was 2.7. The AMM were administered by the parenteral route most commonly (60.6%). The most common AMM prescribed in medicine were ceftriaxone,
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Ciprofloxacin, metronidazole, Anti-tubercular therapy (ATT) and amoxicillin + clavulanate. In Surgery, amoxicillin + clavulanate, ciprofloxacin, Anti-tubercular therapy (ATT), metronidazole and ceftriaxone were most commonly prescribed.

Majority (94.6%) of AMM were prescribed from the EML. The AMM prescribed outside the EML were ofloxacin (8), moxifloxacin (9), clarithromycin (5), piperacillin + tazobactam (25) and clindamycin (11). Three FDCs of AMM were prescribed. They were amoxicillin + clavulanate (112), piperacillin + tazobactam (25), and trimethoprim + sulfamethoxazole (3).

Overall, 8342.3 DDDs of AMM were utilized in both Medicine (5477.8 DDD, 65.7%) and Surgery (2864.5 DDD, 34.3%) inpatients [Tables 5 and 6]. Overall, the AMM with highest utilizations in DDDs were ceftriaxone, ciprofloxacin, amoxicillin + clavulanate [Figure 2].

Antimicrobials were prescribed for therapeutic indication in majority of the cases (78.7%). More patients were prescribed for prophylaxis in surgery. Samples for culture sensitivity were sent in 84 (21%) cases, of which microbiological evidence of infection was established.
Table 5: Utilization (defined daily doses) of antimicrobial medicines in medicine inpatients

| Antimicrobial medicine                           | ATC code | DDDs | DDDs per 100 patient days |
|-------------------------------------------------|----------|------|---------------------------|
| Ceftriaxone, 1000 mg                             | J01DD04  | 1704.1 | 11.6                     |
| Ciprofloxacin, 250 mg                            | J01MA02  | 1405  | 9.62                      |
| Metronidazole, 400 mg                            | J01XD01  | 582.8 | 3.99                      |
| Antitubercular therapy (isoniazid, rifampicin, pyrazinamide, ethambutol) | J04AC01, J04AB02, J04AK01, J04AK02 | 515  | 3.52                      |
| Amoxicillin-clavulunate, 625 mg                  | J01CR02  | 312   | 2.13                      |
| Azithromycin, 1000 mg                            | J01FA10  | 187.2 | 1.28                      |
| Meropenem, 500 mg                                | J01DH02  | 147   | 1.00                      |
| Piperacillin-tazobactam, 3.37 g                  | J01CR05  | 75.4  | 0.51                      |
| Levofloxacin, 500 mg                             | J01MA12  | 74.85 | 0.51                      |
| Amikacin, 250 mg                                 | J01GB06  | 60    | 0.41                      |
| Amoxicillin, 500 mg                              | J01CA04  | 52.6  | 0.38                      |
| Streptomycin, 1000 mg                            | J01GA01  | 44    | 0.30                      |
| Moxifloxacin, 500 mg                             | J01MA14  | 42.8  | 0.27                      |
| Clindamycin, 500 mg                              | J01FF01  | 40    | 0.15                      |
| Doxycycline, 100 mg                              | J01AA02  | 32    | 0.21                      |
| Vancomycin, 500 mg                               | J01XA01  | 26.6  | 0.18                      |
| Benzathine Penicillin, 1.2M units                | J01CE08  | 24    | 0.16                      |
| Acyclovir, 400 mg                                | J05AB01  | 18.4  | 0.12                      |
| Albendazole, 400 mg                              | P02CA03  | 18    | 0.12                      |
| Artesunate, 60 mg                                | P01BE03  | 17.1  | 0.11                      |
| Ofloxacin, 500 mg                                | J01MA01  | 16.83 | 0.11                      |
| Gentamicin, 40 mg                                | D06AX07  | 16    | 0.10                      |
| Cotrimoxazole, 480 mg                            | J01XE01  | 15.5  | 0.10                      |
| Nitrofurantoin, 100 mg                           | J01EE01  | 11    | 0.07                      |
| Erythromycin, 500 mg                             | J01FA01  | 10.8  | 0.07                      |
| Chloroquine, 300 mg                              | P01BA01  | 9.5   | 0.06                      |
| Cefixime, 200 mg                                 | J01DD08  | 8     | 0.05                      |
| Ceftazidime, 200 mg                              | J01DD02  | 6.5   | 0.04                      |
| Ampicillin, 200 mg                               | J01CA01  | 4.8   | 0.03                      |
| **Total**                                        |          | 5477.8 | 37.2                     |

ATC=Anatomical therapeutic chemical, DDDs=Defined daily doses

in 33 (8.5%) samples [Table 7]. The AMM therapy was modified in 15.5% of cases. The main reason for change is lack of response to the therapy. In five patients, the AMM therapy was modified due to the occurrence of adverse medicine reactions. The four adverse medicines reactions reported in the medicine department were as follows: Two cases of hepatotoxicity due to ATT, a case of red man syndrome due to vancomycin and rash caused by ciprofloxacin. The adverse medicines reaction reported from surgery was a hypersensitivity reaction caused by amoxicillin + clavulanate.

**Rationality of antimicrobials used**

Overall, the AMM given was appropriate as per Kunin’s criteria 1 in 352 (88%), criteria 2 in 10 (2.5%), and criteria 3 in 34 (8.5%) patients.

**Expenditure on antimicrobial medicines**

The total cost of medicines in both the departments was INR 1,812,762 with expenditure on AMM being 33.13% of the total [Table 8]. The maximum expenditure was on parenteral AMMs. The average cost of AMMs was INR 1501 per patient. The ABC analysis of expenditure incurred on AMM overall showed that around 74.6% of the expenditure was due to three AMM namely meropenem, piperacillin + tazobactam and ceftriaxone which made up just 9% of the AMM used and 4.8% of the expenditure was spent on 87.5% of the AMM [Table 9]. The remaining 20% of the total expenditure on AMM was spent on 6.1% of the AMM [Figures 3 and 4].

**Discussion**

Availability of AMM utilization data in the community is an essential pre requisite for formulating local AMM use policies and for AMM surveillance. While drug utilization studies (DUS) of AMM are common in the West, the same are not available in India. A systematic review done in the WHO-SEARO region showed that among the 318 DUSs published till 2012, only 67 were from India. Further DUS need to be conducted in similar settings to see for trends and changes in the use of AMM. This study was conducted in a large tertiary care teaching hospital in India, in the national capital New Delhi. We attempted
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To generate AMM utilization and expenditure data which would not only help to formulate a local AMM use policy but also function as a yardstick to assess the impact of any intervention to rationalize use of AMM. A similar study was conducted by the authors 6 years back; however, quantitative estimation of AMM use in terms of DDD was not done and it only focused on inpatients.[20]

The medicine and surgery departments were selected as they have maximum number of admissions and patient visits in the hospital. The demographic characteristics of the patients in both medicine and surgery departments

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### Table 6: Utilization (defined daily doses) of antimicrobial medicines in surgery inpatients

| Antimicrobial medicine                                      | ATC code         | DDDs  | DDDs per 100 patient days |
|-------------------------------------------------------------|------------------|-------|--------------------------|
| Amoxicillin-clavulunate, 625 mg                              | J01CR02          | 715.8 | 6.62                     |
| Ciprofloxacin, 250 mg                                       | J01MA02          | 687.2 | 6.36                     |
| Ceftriaxone, 1000 mg                                        | J01DD04          | 505   | 4.67                     |
| Antibacterial therapy (isoniazid, rifampicin, pyrazinamide, ethambutol) | J04AC01, J04AB02, J04AK01, J04AK02 | 268   | 2.48                     |
| Metronidazole, 400 mg                                       | J01XD01          | 259.7 | 2.40                     |
| Amoxicillin, 500 mg                                         | J01CA04          | 84.5  | 0.78                     |
| Amikacin, 250 mg                                            | J01GB06          | 65.5  | 0.60                     |
| Nitrofurantoin, 100 mg                                      | J01EE01          | 48.5  | 0.44                     |
| Levofloxacin, 500 mg                                        | J01MA12          | 44.8  | 0.41                     |
| Gentamicin, 40 mg                                           | D06AX07          | 38.5  | 0.35                     |
| Benzathine penicillin, 1.2 M units                         | J01CE08          | 27    | 0.24                     |
| Clindamycin, 500 mg                                         | J01FF01          | 22.2  | 0.20                     |
| Meropenem, 500 mg                                           | J01DH02          | 18    | 0.16                     |
| Clarithromycin, 250 mg                                      | J01FA09          | 17.4  | 0.16                     |
| Acyclovir, 400 mg                                           | J05AB01          | 16.4  | 0.15                     |
| Streptomycin, 1000 mg                                       | J01GA01          | 11    | 0.10                     |
| Vancomycin, 500 mg                                          | J01MA01          | 5.5   | 0.05                     |
| Piperacillin-tazobactam, 3.37 g                             | J01CR05          | 7.5   | 0.06                     |
| Ofloxacin, 500 mg                                           | J01MA01          | 6.5   | 0.06                     |
| Albenazole, 400 mg                                          | P02CA03          | 6     | 0.05                     |
| Azithromycin, 1000 mg                                       | J01FA10          | 5.5   | 0.05                     |
| Total                                                       |                  | 2864.5| 26.4                     |

ATC=Anatomical therapeutic chemical, DDDs=Defined daily doses

### Table 7: Antimicrobial use: Indication, availability of microbiological evidence, and reasons for change of therapy

| Variable                                      | Medicine, n (%) | Surgery, n (%) | Total, n (%) |
|-----------------------------------------------|-----------------|----------------|--------------|
| Indication for use                            |                 |                |              |
| Therapeutic                                   | 192 (96)        | 123 (61.5)*    | 315 (78.7)   |
| Prophylactic                                  | 8 (4)           | 77 (38.5)*     | 85 (21.2)    |
| Bacteriological evidence                      | 15 (7.5)        | 18 (9)         | 33 (8.5)     |
| Evidence of infection                         |                 |                |              |
| Clinical                                      | 200             | 200            | 400          |
| Samples sent for culture sensitivity         | 36 (18)         | 48 (24)        | 84 (21)      |
| Change in AMM therapy                        | 46 (74.2)       | 16 (25.9)      | 62           |
| Reasons for change in antimicrobial therapy  |                 |                |              |
| Patient not responding                        | 28 (60.8)       | 5 (31.20)      | 33 (53.2)    |
| Change in diagnosis                          | 10 (21.7)       | 2 (12.5)       | 12 (19.3)    |
| Confirmed culture sensitivity report         | 4 (8.6)         | 8 (50)         | 12 (19.3)    |
| Adverse drug reactions                        | 4 (8.6)         | 1 (6.25)       | 5 (9.6)      |

*P<0.05. AMM=Antimicrobial medicine

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Figure 3: ABC analysis of expenditure on antimicrobials in medicine department (inpatients)
were comparable, except the patient’s duration of stay which was longer in medicine inpatients.

As expected, the overall use of AMM was more in the medicine department in both outpatients and inpatients, since infections are a common cause for patient’s visits in the medicine department. The extent of use of AMM in outpatients (53%) was more than in other studies, where AMM encounters have ranged from 41% to 46.7% in Indian subcontinent.[21‑23]

The use of AMM in inpatients was nearly double of that in outpatients (73% vs. 38%) in this study and majority of patients were prescribed multiple AMM. Possible reason for this could be that serious patients are admitted and infectious etiology is a common reason for morbidity and mortality in the hospital. Among inpatients, the overall percentage use of AMM (73%) in this study appears to be more than the studies conducted in developed countries like Sweden (31%) and developing countries such as Egypt (61%), Indonesia (65%), and Bangladesh (54%).[24‑27]

The use has increased in comparison to a similar study conducted in medicine and surgery inpatients at our hospital 5 years ago.[20]

Overall, amoxicillin + clavulanate (32.1%) were the most commonly prescribed AMM in medicine and surgery outpatients in terms of prescription encounters. In other studies, Amoxicillin was reported as the most frequently used AMM. The reason for the same is not clear as there is the absence of AMM sensitivity data. It can be attributed either to AMR to amoxicillin or to prescriber’s notion that it is more effective in the absence of availability of AMM sensitivity data. The use of metronidazole in surgery outpatients was almost double to that of medicine outpatients. The probable reason could be a higher fraction of encounters with anaerobic infections in surgery than in medicine.

The most commonly prescribed AMM in inpatients in medicine were ceftriaxone, ciprofloxacin, and metronidazole and in surgery were amoxicillin + clavulanate, ciprofloxacin and ceftriaxone. This pattern of use of AMM in inpatients was similar to other studies in India where in the most commonly used AMM were beta lactams followed by fluoroquinolones and aminoglycosides.[28,29]

Among inpatients, parenteral route was the most preferred route for AMM (60%–65%). Thus, there was more use of injectables in this study which should be restricted to emergency care, serious infections, and medicines with poor bioavailability or patients with gastrointestinal dysfunction.

In most cases, AMM therapy was initiated based on clinical evidence with very few samples sent for microbiological testing and even lesser confirming the same. The support of microbiological laboratory services for determining the AMM sensitivity data is of prime importance for determining rational use of

| Table 8: Expenditure on antimicrobial medicines among inpatients (INR) |
|--------------------------|-----------------|-----------------|
|                         | Medicine (INR)  | Surgery (INR)   | Total            |
| Cost of all medicines   | 1,447,281       | 365,481         | 1,812,762        |
| Cost of antimicrobials (%) | 470,444.3 (32.50) | 210,462* (57.58)* | 680,906 (37.50) |
| Cost of AMM per patient, per treatment course (mean) | 2352            | 1052*           | 1501             |
| Expenditure on AMM as per route, total cost (%) | 458,212.4 (97.4) | 206,673.6 (98.2) | 664,886 (97.6) |
| Intravenous             | 9408.8 (0.02)   | 210 (0.1)       | 9618 (1.4)       |
| Intramuscular           | 11,761.1 (2.5)  | 3577.8 (1.7)    | 15,338.9 (2.2)  |
| Oral                    | 376.3 (0.08)    | 0 (0)           | 376.3 (0.05)     |

*P<0.05. AMM=Antimicrobial medicine

| Table 9: ABC analyses of antimicrobial medicine prescribed in medicine and surgery inpatients (INR) |
|--------------------------|-----------------|-----------------|
|                         | Medicine (INR)  | Surgery (INR)   | Overall  |
| Department               | Total expenditure (%) | Total expenditure (%) | Total expenditure (%) |
| AMM (n)                  | A (70%)         | B (20%)         | C (10%) |
| Medicine                 | 3               | 6               | 23     |
| AMM (n)                  | 353,855.2 (74.3) | 98,559.0 (20.7) | 23,726 (5) |
| Surgery                  | 2               | 6               | 13     |
| AMM (n)                  | 120,338 (73.8)  | 25,822 (21.6)   | 8716 (5.4) |
| Overall                  | 3               | 2               | 28     |
| AMM (n)                  | 524,427.7 (74.6)| 145,496 (20.6)  | 33,333 (4.8) |

AMM=Antimicrobial medicine

Overall, amoxicillin + clavulanate (32.1%) were the most commonly prescribed AMM in medicine and surgery outpatients in terms of prescription encounters. In other studies, Amoxicillin was reported as the most frequently used AMM. The reason for the same is not clear as there is the absence of AMM sensitivity data. It can be attributed either to AMR to amoxicillin or to prescriber’s notion that it is more effective in the absence of availability of AMM sensitivity data. The use of metronidazole in surgery outpatients was almost double to that of medicine outpatients. The probable reason could be a higher fraction of encounters with anaerobic infections in surgery than in medicine.

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| AMM (n)                  | 524,427.7 (74.6)| 145,496 (20.6)  | 33,333 (4.8) |

AMM=Antimicrobial medicine

Overall, amoxicillin + clavulanate (32.1%) were the most commonly prescribed AMM in medicine and surgery outpatients in terms of prescription encounters. In other studies, Amoxicillin was reported as the most frequently used AMM. The reason for the same is not clear as there is the absence of AMM sensitivity data. It can be attributed either to AMR to amoxicillin or to prescriber’s notion that it is more effective in the absence of availability of AMM sensitivity data. The use of metronidazole in surgery outpatients was almost double to that of medicine outpatients. The probable reason could be a higher fraction of encounters with anaerobic infections in surgery than in medicine.

The most commonly prescribed AMM in inpatients in medicine were ceftriaxone, ciprofloxacin, and metronidazole and in surgery were amoxicillin + clavulanate, ciprofloxacin and ceftriaxone. This pattern of use of AMM in inpatients was similar to other studies in India where in the most commonly used AMM were beta lactams followed by fluoroquinolones and aminoglycosides.[28,29]

Among inpatients, parenteral route was the most preferred route for AMM (60%–65%). Thus, there was more use of injectables in this study which should be restricted to emergency care, serious infections, and medicines with poor bioavailability or patients with gastrointestinal dysfunction.

In most cases, AMM therapy was initiated based on clinical evidence with very few samples sent for microbiological testing and even lesser confirming the same. The support of microbiological laboratory services for determining the AMM sensitivity data is of prime importance for determining rational use of
AMM. This invariably leads to prescription of multiple AMM as empirical therapy while awaiting laboratory results. Around 80% of the patients received more than one AMM which is more than in a study conducted at Chandigarh (66%). The greater use of AMMs for prophylaxis is expected in surgery. However, this use of AMM as a prophylactic measure is much lesser than that reported in studies conducted in the US and China, wherein the use is as high as 99.3% and 98%, respectively.

Modification in the AMM therapy had to be done in 15.5% of cases, the most common reason being the patient not responding to prescribed treatment. However, in surgery inpatients the most common reason for change in AMM therapy was based on report of culture and sensitivity. Other causes attributed to modification of therapy were the occurrence of adverse reactions and change of provisional diagnosis. These causative factors highlight the problem prescribing physicians are facing due to the lack of hospital AMM sensitivity data. Availability of such vital data on a regular basis could make prescribing of AMM practices rational and justifiable.

Despite lack of microbiological support, majority of the patients received appropriate AMM therapy (88%) which is similar to other studies in Scotland (84%) and Nepal (73.8%). Only one patient’s treatment was placed in category 5. This patient was administered an AMM for pyrexia, the causative factor of which was an early manifestation of transfusion reaction. Hence, AMM therapy was unjustified in that particular scenario. The rationality of individual cases was reasoned with clinicians. In the absence of microbiological evidence of infection and culture sensitivity data, judgment based on clinical acumen and reasoning is heavily relied on in practice.

There was good adherence to the EML among the prescribers as around 97% (outpatients) and 94.6% (inpatients) of the AMM in the outpatients were prescribed from the EML. This WHO prescribing indicator in the present study fared better compared to other studies done in Jamnagar (42%) and in Central India (61.4%). Most of the medicines prescribed outside the EML were irrational medicine combinations and therefore are not part of EML. Prescribing such medicine combinations is indicative of irrational practices and is a violation of Medicines Policy of the Government of Delhi.

Three of the FDCs prescribed to outpatients were irrational combinations, while all FDCs of AMM prescribed to inpatients were rational. These irrational FDCs are not part of the hospital EML. Since only the medicines in the hospital EML would be provided free of cost to patients, the outpatients would have spent money on procuring these medicines. This observation also highlights how the EML can help in rationalizing the use of medicines.

The utilization of AMM was assessed by calculating DDDs. In the present study, total DDDs of AMM in medicine and surgery in patients were 5438.1 and 2864.5, respectively. The DDDs/100 patient days in medicine and surgery were 37.54 and 26.51, respectively. In another study conducted in Kashmir, an analysis of AMM consumption for a duration of 2 months was performed and the total DDDs/100 patient days for systemic use was reported to be 78. However, the results of the AMM consumption cannot be compared with the present study, mainly because of differences in study settings and methodology. Nevertheless, this information will now be used for quantifying AMM use in the health facility.

Overall, 33% of the cost on medicines was incurred on use of AMM. The percentage expenditure incurred on AMM is much more than observed in a study conducted in the UK, where it was reported to be 19%. This stark difference is a manifestation of the high incidence of infectious etiology and excessive consumption of AMM in developing countries.

The ABC analysis of expenditure incurred on AMM overall showed that around 74.6% of the expenditure was due to three AMM namely meropenem, piperacillin + tazobactam and ceftriaxone which made up just 9% of the AMM used and 4.8% of the expenditure was spent on 87.5% of the AMM [Table 9]. This trend reflects that maximum expenditure was incurred due to three AMMs used only in few patients while comparatively less expenditure was incurred on AMMs that were prescribed commonly. Thus, monitoring of expensive AMM is of prime concern as their use can significantly affect the budget. A large proportion of expenditure is being incurred on expensive AMM used disproportionately in a small subset of patient population. These AMM would require more intensive surveillance.

Comparing the results to the previous study, there has been no significant change in the utilization pattern of AMM in the medicine and surgery inpatients. The practice of clinicians prescribing AMM without microbiological confirmation still persists. However, a small trend towards rational use of medicines is seen. The number of individual AMM used has reduced from 46 to 33. There is also increased adherence to EML (74% vs. 98%), and a decline in use of intravenous route (70.6% vs. 60.6%). This rational use of AMM has resulted in lesser expenditure being incurred on AMM compared to the
previous study (54 vs. 33%). The reasons for this could be the government policy and repeated reminders to doctors to prescribe only from the hospital EML.

The problem of AMR has also been highlighted by the government. The hospital has formulated an infection control committee. All these factors have helped in bringing the change in rational use of AMM in the hospital. However, a more organized program to rationalize the use of AMM is required.

Conclusion

Doctors are prescribing AMM empirically based on their clinical acumen rather than availability of microbiological sensitivity data. A large expenditure is being incurred on a few AMM prescribed to small percentage of patients. There is a need for formulation and implementation of an AMM policy as a first step to improve use of AMM within the hospital.

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Conflicts of interest
There are no conflicts of interest.

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