

## ASSESSMENT OF DRUG UTILIZATION PATTERN OF ERYTHROPOIETIN IN PATIENTS WITH ANAEMIA OF CHRONIC KIDNEY DISEASE AND ON HAEMODIALYSIS

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**ABSTRACT: OBJECTIVES:** To access the efficacy of erythropoietin in patients with chronic kidney disease and on haemodialysis, compare the efficacy via intravenous route relative to the subcutaneous route, Evaluate Adverse Events that occur during the course of therapy, Assess Patients Perceptions of Health Related Quality of Life. **MATERIAL & METHODS:** Patients with Anemia of Chronic Kidney Disease and on haemodialysis were screened and enrolled. These patients were traced retrospectively to the date of initiation of therapy with erythropoietin and were followed prospectively. The study duration was 12 months. **RESULTS:** A total of 108 patients were enrolled. Haemoglobin increased to  $9.8 \pm 1.9$ g/dl in the erythropoietin group and fell to  $8.3 \pm 2.2$ g/dl in the iron only group at end of study. Mean haemoglobin for the IV group was  $9.2 \pm 1.9$ g/dl and increased to  $10.1 \pm 2.1$ g/dl in the SC group at the end of study. Blood transfusions were required in 17 patients of the Iron Only Group and 3 patients in the epo+iron group. All of the patients were hypertensive with 37 patients treated with multiple drugs. 14 patients in the epo+iron group had IHD related event. 6 patients had failed AVFs. Quality of life with respect to ESRD targeted scales shows that patients in the erythropoietin group had an improved quality of life. **SUMMARY & CONCLUSION:** Erythropoietin +Iron were more effective in increasing and maintaining haemoglobin levels than Iron alone. The SC route proves more efficacious. Patients treated with epoetin had increased incidence of an adverse event. Patients not treated with erythropoietin required blood transfusions. Patients with ESRD have higher QOL when treated with erythropoietin.

**KEYWORDS:** Erythropoietin, Chronic Kidney Disease, Anemia of CKD.

**INTRODUCTION:** The irrational use of antibiotics can be the cause for a number of patients undergoing treatment that does not lead to complete remission. Unnecessary prescription of drugs that cover a broader spectrum of antimicrobial activity leads to development of resistance to antibiotics, adverse effects and economic burden on patients and the society. In spite of efforts by organizations like the WHO to curb irrational prescribing it still remains a major problem especially amongst surgical inpatients.

The problem is further complicated by the lack of governance over prescribers leading to an increasing number of quacks and underqualified prescribers and lack of control over dispensing of antibiotics from pharmacies. Rational use of drugs requires that patients receive medicines appropriate to their clinical needs, in appropriate doses, for adequate period of time and at that lowest possible cost.<sup>1</sup> Antibiotics are one of the most commonly prescribed medications by clinicians especially in the Surgical in patient setup with one study showing Amoxicillin and Clavulanic acid as the most commonly used drug whilst another study documented Amikacin and third generation Cephalosporins as the most commonly prescribed drugs.<sup>2,3</sup>

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Amongst patients admitted with surgical problems, Skin and Soft Tissue Infections (SSTIs) like abscess, furuncles and cellulitis are common. The major modality of treatment is antimicrobial therapy with/without surgical intervention.

We conducted this study with the aim to study the prescribing patterns of antibiotics in patients admitted to a private surgical set up with clinically established diagnosis of skin and soft tissue infections.

### OBJECTIVES:

- To study prescribing patterns of antibiotics in skin and soft tissue infections.
- Number of Antibiotics per prescription.
- Number of encounters resulting in prescription of antibiotic by parenteral route.
- Duration of hospital stay of patients.
- Key factors that govern the choice of prescription of an antibiotic like severity of SSTI, route of administration and category of antibiotic used were assessed.

### METHODOLOGY:

- A cross sectional retrospective study was carried out in a private surgical set up in Mumbai.
- Patients with clinical diagnosis of SSTIs who were admitted for than 1 day were included in the study. The clinical records and files of the 118 in-patients over 3 years from January 2008 to December 2011 were analyzed.

### The Parameters Recorded were:

1. Patient demographics-age, sex, marital status.
2. Clinical diagnosis of SSTI.
3. Clinical findings- heart rate, blood pressure, respiratory rate, local and systemic signs of infection.
4. Details of relevant investigations- like bacterial culture and antibiotic sensitivity, blood sugar.
5. Management- surgical or conservative.
6. Route of administration of drugs.
7. Number of days of hospital stay.

SSTIs are best classified according to the anatomical site of infection. Alternatively, they may be classified according to their microbial aetiology or by severity. The practice guidelines of the Infectious Diseases Society of America (IDSA) for the diagnosis and management of skin and soft tissue infections<sup>6</sup> classifies SSTIs into five categories, comprising superficial, uncomplicated infection (Includes impetigo, erysipelas and cellulitis), necrotizing infection, infections associated with bites and animal contact, surgical site infections and infections in the immune compromised host. By contrast, Eron et al.<sup>4</sup> classify these infections according to the severity of local and systemic signs, thereby developing a system that guides the clinical management and treatment decisions for patients with SSTIs. They divide patients with SSTIs into four classes based on the criteria.

Crest modification of Eron's severity assessment of SSTIs and appropriate therapy is as follows.<sup>5</sup>

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**Class I:** CREST definition- patients have no signs of systemic toxicity and no uncontrolled co-morbidities; and study definition, no recorded significant co-morbidity (peripheral vascular disease, chronic venous insufficiency, Diabetes or morbid obesity), no sepsis and SEWS (Standardized early warning score) <4.

**Appropriate Treatment:** Oral therapy active against staphylococcus aureus or streptococcus pyogens.

**Class II:** CREST definition, patients are either systemically ill or systemically well but with co-morbidity such as peripheral vascular disease, chronic venous insufficiency, Diabetes, Hypertension, or morbid obesity, which may complicate or delay resolution of their infection; and study definition, documentation of one or more significant co-morbidities (Peripheral vascular disease, chronic venous insufficiency, Diabetes, Hypertension or morbid obesity) but no sepsis and SEWS <4.

**Appropriate Treatment:** Intravenous therapy against S. aureus and S. pyogens.

**Class III:** CREST definition, patients may have a significant systemic upset such as acute confusion, tachycardia, tachypnoea or hypotension or may have unstable co-morbidities that may interfere with response to therapy or have a limb-threatening infection due to vascular compromise; and study definition, sepsis but SEWS <4.

**Appropriate Treatment:** Intravenous therapy against S. aureus and S. pyogens.

**Class IV:** CREST definition, patients have sepsis syndrome or severe life-threatening infection such as necrotizing fasciitis; and study definition, sepsis with SEWS ≥4.

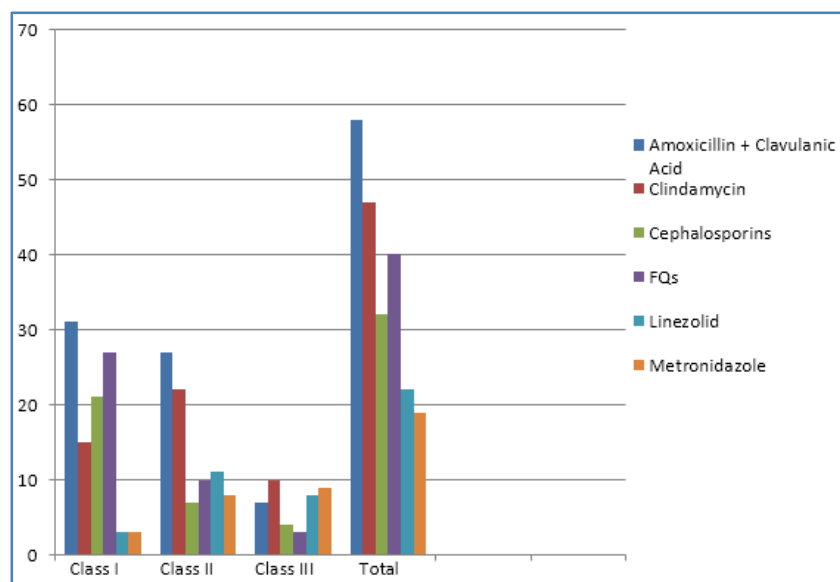
Appropriate treatment- intravenous therapy against S. aureus and S. pyogens, anaerobic bacteria, gram-negative bacteria that includes a drug that reduces toxin production by S. Pyogens (Clindamycin and Linezolid)

**RESULTS:** Patient distribution across Classes of infections (Severity assessment by CREST criteria).

CLASS	NO. OF PATIENTS
CLASS 1	56
CLASS 2	38
CLASS 3	24
<b>TOTAL NO. OF PATIENTS</b>	<b>118</b>

Table 1

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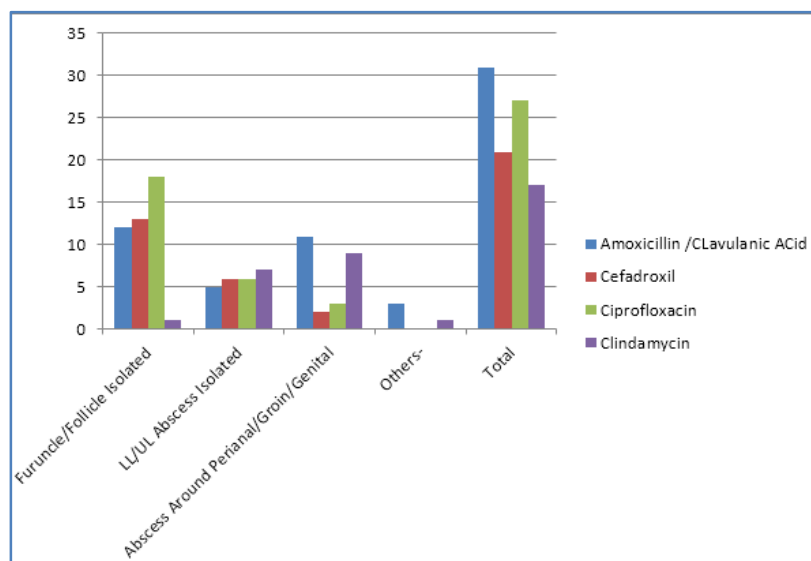


**ANTIBIOTICS USE ACROSS SSTI SEVERITY CLASSES**

Penicillins (Amoxycillin+Clavulanic acid), Lincosamides (Clindamycin), Cephalosporins and Fluoroquinolones were the most commonly prescribed antibiotics across all classes. Amoxicillin+Clavulanic acid was used in 31% patients in Class 1 and 2, with a reduction of its use in only 17% of patients in class 3 category.

The use of Linezolid and Metronidazole was 3% each in class 1, increasing to 13% and 8% in class 2 and 18% and 21% in class 3 respectively.

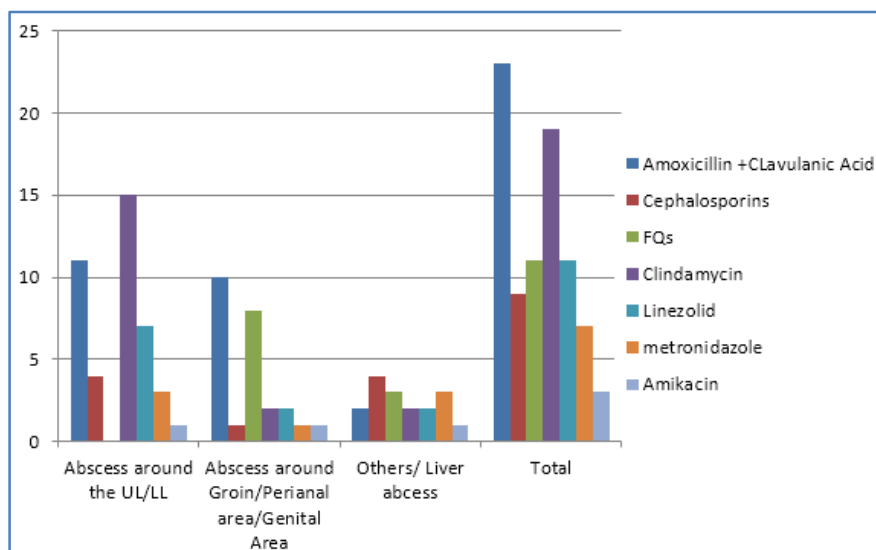
The use of Fluoroquinolones was higher in class 1 and reduced in class 2 and 3, while use of Clindamycin was higher in class 2 and 3 patients.



**ANTIBIOTICS USE ACROSS AETIOLOGICAL SUBTYPES IN CLASS 1**

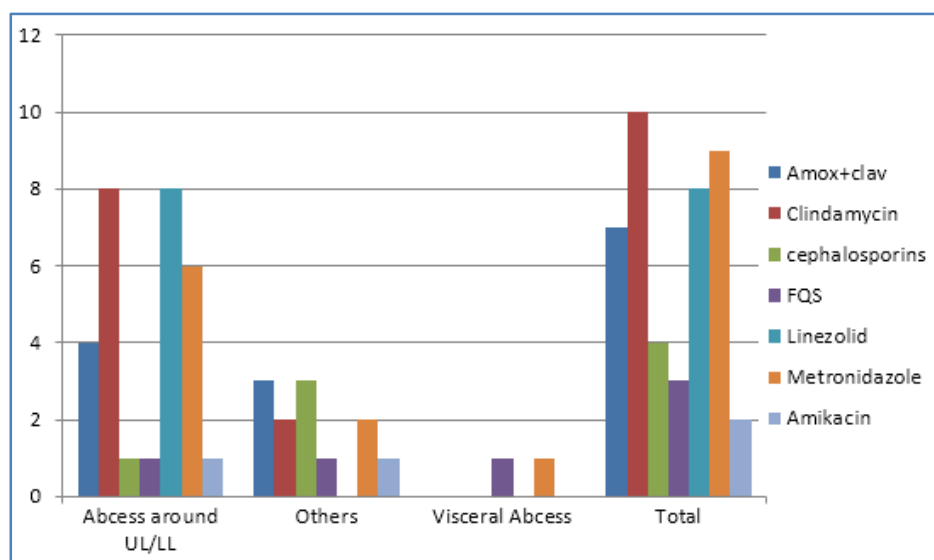
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Ciprofloxacin was used in 41% patients in isolated follicle/ furuncle. Clindamycin was used in 30% of patients with abscess in upper or lower limbs. The use of Amoxycillin+Clavulanic acid was preferred in patients with abscess around genital/genital/ perianal areas.



### ANTIBIOTICS USE ACROSS AETIOLOGICAL SUBTYPES IN CLASS 2

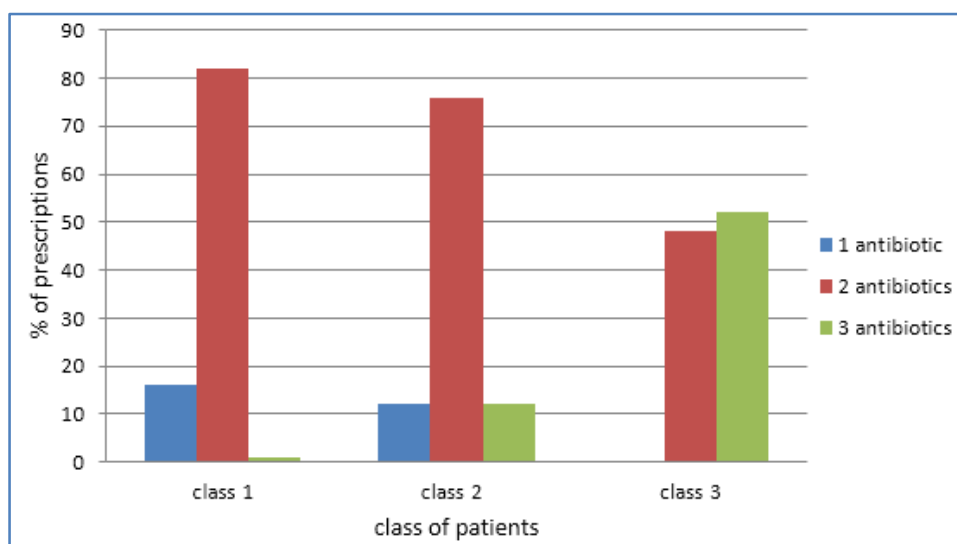
Clindamycin was used in 15% patients with abscess in upper or lower limbs, whilst its use reduced in patients with abscess around genital areas. Amoxycillin+Clavulanic acid was preferred in patients with groin abscess followed by Fluoroquinolones. Linezolid was prescribed commonly to patients with abscess around limbs.



### ANTIBIOTICS USE ACROSS AETIOLOGICAL SUBTYPES IN CLASS 3

In patients with class 3 severity, Clindamycin and Linezolid were preferred in patients with abscess around limbs.

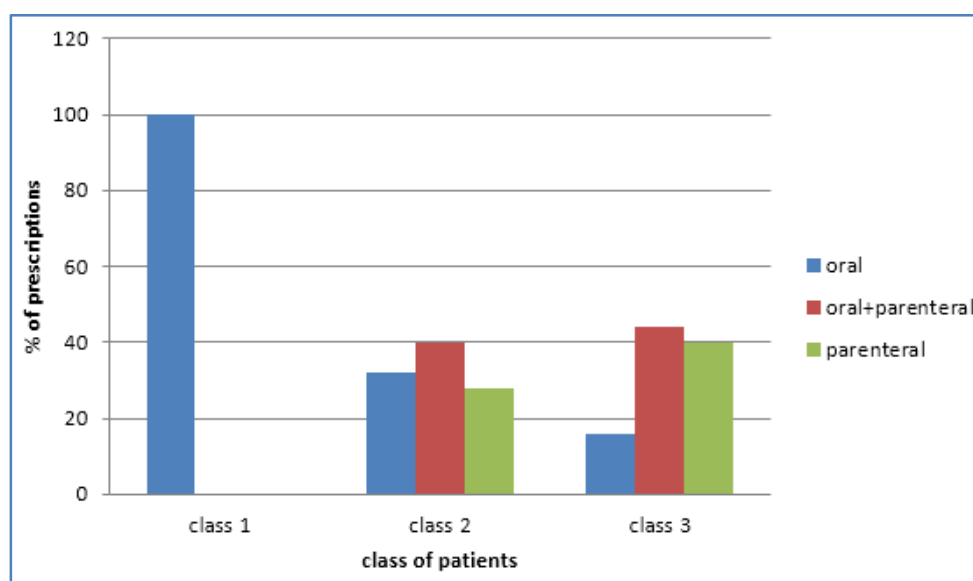
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### NUMBER OF ANTIBIOTICS PER PRESCRIPTION

Physicians commonly prescribed a combination of 2 antibiotics to patients. In patients with class 3 severity, 3 antibiotics were prescribed to 52% of patients.

Average number of antibiotics per prescription was 2.03.



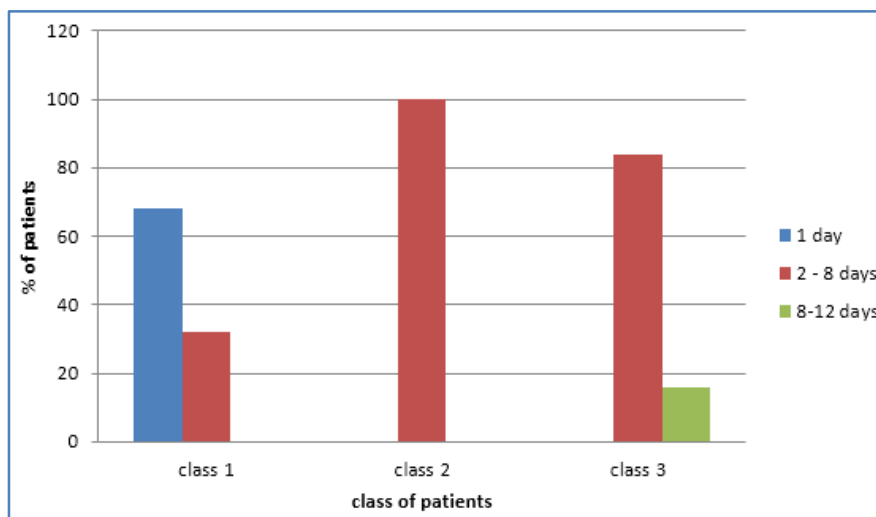
### ROUTE OF ADMINISTRATION OF DRUGS

For class 1, all patients were treated with oral empiric antibiotic drugs with or without surgical drainage procedure. These findings are consistent with the IDSA/CREST guidelines

For class 2, 28% patients were treated with parenteral therapy, with 40% receiving both oral and parenteral therapy and 32% patients receiving only oral therapy. These findings suggest a preference of oral route which deviates from IDSA/CREST guidelines which recommend parenteral antibiotics for class 2 severity.

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For class 3, oral+parenteral drugs were prescribed to 44% patients followed by only parenteral therapy to 40 % patients.



### DURATION OF HOSPITAL STAY OF PATIENTS

68% patients belonging to class 1 were admitted to the hospital for just 1 day.

All patients in class 2 category were admitted between 2-8 days

16% of patients in class 3 were admitted more than 8 days.

Average duration of hospital stay of patients suffering from SSTI was 2.98 days.

**DISCUSSION:** There was an increase in the number of antibiotics prescribed with wider spectrum antibiotics used as the severity of infection increased.

Amoxicillin+Clavulanic acid, Clindamycin and Cephalosporins were the preferred antibiotics in patients belonging to class 1. These choices of antibiotics are consistent from recommendations by previous studies.<sup>6</sup> Fluoroquinolones were prescribed to 27% patients with class 1 SSTIs diagnosed with isolated furuncle/ hair follicle infection/Epidermoid cyst. This was considered inappropriate by IDSA guidelines.<sup>6</sup>

Linezolid and Metronidazole were used in patients with class 2 and class 3 infections. This is consistent with findings of previous studies which recommends use of Linezolid in suspected MRSA infections.<sup>4</sup>

Clindamycin was the preferred agent for SSTIs around the limbs and genitals in class 1 patients.

In patients of class 2 Clindamycin along with Amoxycillin+Clavulanic acid were preferred drugs.

These findings are consistent with recommendations from IDSA.<sup>6</sup>

Amikacin was used in class 2 and class 3 patients to treat infections around the lower limb and groin/ perianal area where other antibiotics were not effective. It was given as local injection over the wound in 1 patient. In all other patients it was given parenterally.

In our study testing for bacteriological culture and antibiotic sensitivity was inadequate and was done in only 5 patients. All the antibiotics except Amikacin were prescribed by brand name.

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An evidence based approach to antibiotic prescribing using standard treatment guidelines should be adopted. It should be based on local as well as national/ international evidence of common antibiotic sensitivity patterns and must be under continuous scrutiny.<sup>7</sup>

The guidelines for antibiotic use should be syndrome based and different parameters like specific area of infection/aetiological subtype of infections should be taken into consideration with probable alternatives for conditions treated empirically.<sup>8</sup>

The system of antibiotic order forms in the hospital is recommended. And infectious diseases specialist consultation is necessary.<sup>7</sup>

An antibiotic usage team should be set up and there should be regular surveillance of antibiotic resistance patterns in the hospital.<sup>9</sup>

### REFERENCES:

1. World Health Organisation. Introduction to drug utilization research. Geneva: World Health Organisation; 2003.
2. Salman MT, Akram MF, Rahman S, Khan FA, Haseen MA, Khan SW. Drug Prescribing Pattern in Surgical Wards of a Teaching Hospital in North India. *Indian Journal for the Practising Doctor*. 2008; 5 (2).
3. Ravi P. Shankar, K. Sen Pranab, Dinesh K. Upadhyay, Arun K. Dubey, P. Subish. Drug utilization among surgical outpatients. *TMJ*. 2006; 56, (2-3):230-234.
4. Lawrence J. Eron, Benjamin A. Lipsky, Donald E. Low, Dilip Nathwani, Alan D. Tice<sup>1</sup> and Gregory A. Volturo. Managing skin and soft tissue infections: expert panel recommendations on key decision points *Journal of Antimicrobial Chemotherapy*. 2003; 52, Suppl. S1, i3-i17.
5. Charis Marwick et al. Severity assessment of skin and soft tissue infections: cohort study of management and outcomes for hospitalized patients. *J Antimicrob Chemother* 2011; 66: 387-397.
6. Dennis L Stevens et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. *Clinical infectious diseases*. 2014; 1-43.
7. Gordon D. Schiff, Mary Wisniewski, Improving Inpatient Antibiotic Prescribing: Insights from Participation in a National Collaborative. *Journal on quality improvement*. 2001; 27 (8).
8. Marivyl Javato-Laxer et al. Antimicrobial prescribing patterns in hospital: Determinants and proposed interventions. *Phil j microbial infectious diseases*. 1989; 18 (2): 41-46.
9. Sujith J. Chandy, Joy Sarojini Michael, Balaji Veeraraghavan, O.C. Abraham, Sagar S. Bachhav and Nilima A. Kshirsagar. ICMR programme on Antibiotic Stewardship, Prevention of Infection & Control (ASPIC) *Indian J Med Res* 139, February 2014; 226-230.



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