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## Antibiotic Utilization Pattern In LSCS Patients

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### ABSTRACT

Cesarean surgical site infections can be prevented by proper preoperative antibiotic prophylaxis. Differences in antibiotic selection in clinical practice exist according to clinicians preferences despite clear guidelines on preoperative antibiotic prophylaxis. The present study thus attempted to understand the antibiotic usage pattern among Lower segment Caesarian section (LSCS) patients in Hyderabad. Subjects for study were patients attending private hospitals in Hyderabad. Case records of LSCS patients who were prescribed antibiotics were used for extraction of relevant data. Other gynecological patients were excluded from the study. The mean age of LSCS patients was 24.57 years. The average number of antibiotics per patient was 2.2. The average number of other drugs per encounter was 6.45. The most commonly prescribed antibiotic was Ceftriaxone followed by Metronidazole. More than 80% of infections were treated with a combination of antimicrobials. In present study, all antibiotics were prescribed in generic name. Polypharmacy was evident from the study. All the antibiotics were given in multiple doses and the administration of antibiotics were given before incision in all patients. Considering spectrum of activity, sensitivity against resistant pathogens and less toxicity, third generation cephalosporins, especially ceftriaxone has been widely used in India for surgical prophylaxis. The common use of ceftriazone and metronidazole could be related to the possibility of mixed infections in LSCS patients. The overall antibiotic usage in LSCS patients were acceptable as per WHO "World Health Organization" standards and the general gynecological practice around the globe. Properly designed studies to assess safety and efficacy of single dose vs multiple dose of antibiotics, pre and post incision antibiotic administration is need of the hour.

**Keywords:** Antimicrobials, Empirical, Prophylactic use, Cesarean Section, LSCS

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## INTRODUCTION

Reproductive health caught the global eye in 1980s, with the launch of Safe Motherhood Initiative, Nairobi in 1987. Since then several National and International initiatives have been adopted to reduce the unacceptable maternal deaths, especially in low resource countries. Based on World Health Organization Trends in maternal mortality from 1990 to 2013, of the total maternal deaths worldwide, at the country level, two countries accounted for one-third of global maternal deaths: India (19%, n = 56000) and Nigeria (14%, n = 40000).<sup>1</sup>

As per the millennium development goals (MDG), India aimed at reducing maternal mortality ratio (MMR) by 75% from 1990 till 2015. The MMR of India has reduced from 560/lakh live births in 1990 to 167/lakh live births in 2011-2013 i.e. a 70.17% decline. <sup>2</sup> Among the maternal mortality, about one third is due to bacterial infections during labour and the puerperium. Most of the estimated 75,000 maternal deaths occurring worldwide yearly as a result of infections are recorded in low-income countries.<sup>3</sup>

Compared to Women who deliver vaginally, LSCS patients are 5-20 times more predisposed to postpartum infections. The incidence of infection varies widely from 2.5% to 20.5% and 40 to 75% in developed countries and developing countries respectively.<sup>4</sup> More distressing is, due to maternal infections, long-term disabilities such as chronic pelvic pain, fallopian tube blockage and secondary infertility could occur in addition to deaths This sort of infections also has a considerable impact on newborn mortality, and an estimated 1 million newborn deaths occur annually.<sup>3</sup>

The use of antimicrobial prophylaxis for caesarean section has been shown to be effective in reducing postoperative morbidity, cost and duration of hospitalization.<sup>5</sup> Antimicrobial usage in the above setting becomes inevitable but should be restricted. The judicious use of these drugs can prevent post-partum infection of the mother and neonate and reduce incidence of adverse drug reactions. The present study was performed to assess the usage of antimicrobials in 100 women undergoing caesarean section

## MATERIALS AND METHOD

### *Population and health care setting*

A quantitative, observational study was undertaken in patients attending private gynecology health care facilities located at Hyderabad, Telangana state, India for three months (Jan – Mar 2019). The hospitals include Lifeline multispecialty hospital, Amma multispecialty hospital, Ganga Nursing home, and Mamatha Nursing home. The data from case records of patients from the Gynecology ward during the study period were taken up for analysis, and the data were noted in a preformed pro

forma. The demographic details of the patients were recorded. The date of admission and discharge, along with the diagnosis written in discharge summary was duly noted. Particulars like name, dose, frequency, duration and route of administration and number of drugs prescribed per admission were documented. Data collected were entered in a prescribed format, and subjected to interpretation and analysis.

The following drug use indicators were assessed using the WHO guidelines on investigation of drug use in health care facilities:

- Average number of drugs per prescription,
- Percentage of encounters with antibiotics
- Percentage of drugs prescribed by generic name,
- Percentage of drugs prescribed from essential drug list
- Percentage of encounters with injection.

Intravenous fluids, blood transfusion and nutritional preparations were not included in the study.

#### ***Inclusion criteria***

- Patients who are in the age group of 18-40 years
- Patients who are admitted for Caesarean deliveries
- All patients receiving/not receiving antibiotic for therapeutic or prophylactic purpose.

#### ***Exclusion criteria***

- Normal delivery Patients
- Patients who are already on antibiotic therapy for any infections.
- Suffering from any serious disease such as unstable coronary heart disease, heart failure, advanced kidney or liver failure.
- Those with specific infectious diseases including tuberculosis, malaria, Leprosy, fungal and viral infections.

## **RESULTS AND DISCUSSION**

In our study, we found out that mean age of paediatric patients was 24.57 yrs (Table-1) and the maximum patients were under the age group of 20-25 (Table 2). All patients were exposed to more than one drug and our results showed tendency of polypharmacy with maximum number of prescriptions. The prescriptions were further analysed for various prescribing indicators as laid down by WHO (Table 1). The average number of antibiotics per patient was 2.2 and the duration of treatment were 5.16 (Table-1). The average number of other drugs per encounter was 6.45 (Table-1). All patients received the drug through injectable mode (8.65) (Table-1). There were only three

FDC (Fixed dose combinations). Among the prescribed drugs, around 50% of the drugs (6.69) come under essential drug list (Table-1). It is surprise to note that, not even a single drug was prescribed on their generic name. The maximum numbers of patients were prescribed with 2 antibiotics (Table 3) and very less patients were prescribed with 1, 2 and 4 antibiotics.

The most common antibiotics prescribed were ceftriaxone and metronidazole (Table 4).

Among the class of antibiotics, cephalosporins and nitroimidazole were the most commonly prescribed alone and in combination (Table 5 & 6). All the antibiotics were given in multiple doses and the administration of antibiotics were given before incision in all patients (Table 6).

The development of clinical infection is dependent on a complex balance between host defense mechanisms and bacterial virulence factors. Cesarean delivery alters this balance so as to predispose the patient to infection. During labor and abdominal delivery, the endometrium and peritoneal cavity invariably are contaminated with large numbers of highly pathogenic aerobic and anaerobic bacteria.<sup>6</sup>

WHO recommends the use of prophylactic broad spectrum antibiotics for women undergoing caesarean section which are effective against the microorganisms associated with endometritis, urinary tract and wound infections.<sup>7</sup> Ideally, for prophylaxis, a drug regimen should be Proven effective in well-designed prospective, randomized, double-blind clinical trials, active against the majority of pathogens likely to be involved, attain adequate serum and tissue levels throughout the procedure, not associated with the development of antimicrobial resistance, inexpensive and well-tolerated.<sup>8</sup>

For caesarean section, WHO recommends a single dose of first generation cephalosporin or penicillin as antibiotic prophylaxis in preference to other classes of antibiotics.<sup>3</sup> This is based on the evidence on effectiveness of antibiotics that came largely from trials that tested first-generation cephalosporin or penicillin. A Cochrane review conducted on the comparative effectiveness of single cephalosporin versus single penicillin (13 trials, 4010 women) found no significant differences between cephalosporin and penicillin regimens for endometritis, maternal febrile morbidity, wound infection, and urinary tract infection.<sup>3</sup> In support of above findings, a small trial done in 60 Indian patients of elective cesarean delivery, identified that broad spectrum amoxicillin-clavulanic acid was not superior to cefazolin in the prevention of postoperative infection when given as prophylaxis.<sup>9</sup> In contrary, ACOG guidelines recommend a narrow spectrum 1st generation cephalosporin (Cefazolin) over Ampicillin as the regimen of choice because of increasing microbial resistance to the latter generally after cord clamping.<sup>8</sup> Similarly, the general clinical practice in Indi and the current study (Table 5) supports the use of cephalosporin.

In the current study, the most commonly prescribed antibiotic was ceftriazone (Table 4), a third generation cephalosporin's, which is in contrast with the WHO recommendations. The reason for not following recommendation has been explored. In general<sup>6</sup>, First generations have good activity against a wide spectrum of gram positive bacteria including penicillinase producing but not methicillin resistant staphylococci. Enterococci are however resistant. Activity against gram negative is modest. They are available in both oral and parenteral forms. In this group, Cefazolin has widely used as a prophylactic drug in high risk elective operations. The major advantages of second generation cephalosporin's are improved activity against important gram negative organisms. Unique feature is its activity against *Haemophilus influenzae* including strains producing beta lactamases. Not active against *Pseudomonas*, *proteus* and enterococci. Third generation cephalosporin's are active against gram-positive and gram -negative microorganisms. It is stable to beta-lactamase produced by many organisms, and has good activity against beta-lactamase producing organisms. Some of the drugs in this class have been suggested as primary single therapy for infections such as nosocomial pneumonia and peritonitis. The major advantage of these drugs over combination of aminoglycosides with earlier generation cephalosporin for infections is lack of toxicity and elimination of need to monitor drug levels. Toxic side effects are unusual. Fourth generations have a very broad spectrum of activity. Hence, among the four generations, considering spectrum of activity, sensitivity against resistant pathogens and less toxicity, third generation cephalosporins, especially ceftriaxone has been widely used in India for surgical prophylaxis.

In the current study, along with ceftriaxone, metronidazole (Table 6) is added to almost all patients. Though there is no strong clinical recommendation, the usage seems to be based on clinical evidence. Actually, the post caesarean infections are usually poly-microbial, involving aerobic and anaerobic organisms.<sup>4,10</sup> Amongst the aerobic bacterial agents causing surgical site infection in caesarean section patients, enteric gram negative bacilli are the most common followed by enterococci and group B streptococci. Clostridia and *Bacteroides* spp. are commonly isolated anaerobic organisms.<sup>10</sup> Considering that the postoperative caesarean section infections could be polymicrobial, the treatment demands addressing both agents, as evidenced by the current study. Further, clinical studies support that extended spectrum regimens (e.g.-a regimen involving the use of both the standard narrow spectrum antibiotics in addition to a second antibiotic of a different class e.g. azithromycin, gentamycin, metronidazole) are significantly more effective in reducing post caesarean infections (by 30-60%) and shortening of hospital stay (and cost) than narrow spectrum agent alone. Studies reveal that the most frequently prescribed antimicrobial combinations were cefotaxime with metronidazole (11.5%) and ceftriaxone with metronidazole (4.4%).<sup>11</sup> Though the combination

enhance the synergistic effect, the chances of enhancing resistant strains, super infections, greater toxicity and increased financial burden cannot be ignored.

Next comes the duration of antimicrobial combinations, as studies support single dose and multiple doses of combination antibiotics. The present study support multiple dose of combination antibiotics for an average duration of 5 days have been given for all LSCS patients (Table 6). Some studies supports the use of single dose of cephalosporin plus metronidazole<sup>8</sup>, while other studies support multiple doses.<sup>11</sup> Detailed studies has to be done to evaluate the safety and efficacy of single dose vs multiple doses of combination antibiotics in LSCS patients.

In 2011, the National Institute for Health and Care Excellence (NICE) revised their guidance on the timing of intravenous prophylactic antibiotic administration for caesarean section, advising that antibiotics should be given prior to skin incision. This change has recently been supported by a Cochrane review which advises administration of antibiotics 60 minutes prior to incision to prevent maternal postpartum infectious morbidity.<sup>7</sup> In line with international recommendation, in our current study (Table 6), all patients received antibiotics prior to skin incision. This pattern of antibiotic utilization raises an inevitable doubt about the impact of antibiotics entering baby's circulation before birth.<sup>7</sup> Because, there is growing awareness of the importance of microbes and the immune system as aetiological agents in human disease. This immune system is based on the composition of early microbial colonization in the baby. Administration of antibiotics prior to incision may impact the microbial colonization and the patients are at increased risk of diseases such as atopic dermatitis, inflammatory bowel disease and Type 1 diabetes. As there is no clear clinical evidence to support the above fact, consideration has to be given for proper study designs to assess long term outcomes.

**Table 1: Demographic and Prescription Pattern**

<b>Particulars</b>	<b>Mean (SD)</b>
Age	24.57 (3.62)
Duration of Treatment	5.16 (0.78)
No. of antibiotics	2.2 (0.82)
Total number of other drugs per prescription	6.45 (1.39)
Number of injectables per prescriptions	8.65 (1.57)
FDC	12 (0)
Essential drug list	3.69 (1.07)
Generics	0

**Table 2: LSCS Patients Age Group**

<b>Age Group</b>	<b>No of Patients</b>
Less than 20 Years	4
20 to 25 Years	64
More than 25 Years	32

**Table 3: Number of Antibiotics per Prescriptions**

<b>Antibiotics</b>	<b>No of Patients</b>
Prescription with 1 antibiotic	12
Prescription with 2 antibiotic	68
Prescription with 3 antibiotic	12
Prescription with 4 antibiotic	8

**Table 4: Antibiotics Prescriptions**

<b>Antibiotic</b>	<b>No of Prescriptions</b>
Ceftriaxone sodium	18
Metonidazole	24
Amikacin	2
Ciprofloxacin	9
Azithromycin	1
Cefuroxime	1

**Table 5: Antibiotics class Prescriptions**

<b>Antibiotic</b>	<b>No of Prescriptions</b>
Cephalosporins	18
Nitroimidazole	24
Aminoglycoside	2
Fluroquinilone	9
Macrolide	1

**Table 6: Clinical course of Prescriptions**

<b>Particulars</b>	<b>No. of Prescriptions</b>
Ceftriaxone+ Metonidazole	80
Cefuroxime + Metronidazole	12
Ciprofloxacin + Metronidazole	0
cephalosporins alone and no Metronidazole	4
Metronidazole alone and no cephalosporins	4
Single dose of antibiotics	0
Multiple dose of antibiotics	100
Administration of antibiotics before Incision	100
Administration of antibiotics after Incision & umbilical cord clamping	0

## CONCLUSION

The overall antibiotic usage in LSCS patients were acceptable as per WHO standards and the general gynecological practice around the globe. Properly designed studies to access safety and efficacy of single dose vs multiple dose of antibiotics, pre and post incision antibiotic administration is need of the hour.



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