



## ORIGINAL ARTICLE

### Antibiotic prescribing pattern in cesarean section

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#### Abstract

Use of antimicrobials in caesarean section has become an accepted practice to minimize the incidence of postoperative complications. Not many studies are available in Bangladesh regarding the using pattern of antibiotics in caesarean section. The objectives of the study was to find out the pattern of use of antibiotic prophylaxis in caesarean section and also the frequency of postoperative morbidity. The prospective cross-sectional study included 356 patients undergoing caesarean section in Prime Medical College Hospital, Rangpur and 10 different private clinics in Rangpur city. Patients demographics, perioperative data, antibiotic used with dosage and schedules were recorded. Investigations like pus, blood and urine culture and sensitivity were recorded for patients with postoperative complications. Change of antimicrobial following culture sensitivity report was noted. Most of the patients, 197 (55.3%), came from lower middle socioeconomic status. Major indication of cesarean section was emergency in 314 (88.2%) patients. The use of third generation cephalosporin (ceftriaxone) in majority of the patients, 209 (58.7%), was observed. Two drugs combination commonly included third generation cephalosporin and metronidazole, and in addition gentamicin was added when three drugs combination was used. Fifty five (15.5%) patients had postoperative complications which included fever, wound infection, urinary tract infection and endometritis. The mean duration (SD) of antibiotic administration was 12.4 (3.5) days in infected patients and 8.0 (2.1) days in non-infected patients, and the difference was statistically significant ( $p < 0.01$ ). The mean duration (SD) of hospital stay was 15.4 (5.5) and 9.1 (3.9) days for infected and non-infected patients, respectively; and the difference was statistically significant ( $p < 0.01$ ). Isolated micro-organisms from wound infection, urinary tract infection and lochia were gram-negative, and Escherichia coli, 16 (41.0%), was the common which was resistant to third generation cephalosporin and sensitive to amikacin. Obstetricians should utilize clinically effective antibiotics. Whenever possible, single drug rather than combination therapy should be used. Periodic surveillance of antimicrobial prophylaxis is essential to detect the emergence of antibiotic resistance.

**Key words:** Antibiotics, cesarean section, postoperative infections.

#### Introduction

There is an increase in the incidence of cesarean section and has risen steadily over the past two decades.<sup>1</sup> Now it is the most

commonly performed major surgical procedure.<sup>2</sup> Cesarean section rates an average greater than 20% in the developed world and makes up a similar percentage in

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hospital deliveries in developing countries. Infectious complications that occur after cesarean delivery are an important and substantial cause of maternal morbidity and are associated with a significant increase in hospital stay.<sup>3</sup> Major challenge for obstetricians dealing with parturient have been the potential occurrence of serious infections during the postpartum period. Infectious morbidity is the most common complication following cesarean section with reported rates ranging from 18% to 83%.<sup>4-7</sup> Women undergoing cesarean delivery have significant incidence of many infectious complications; including fever, bacteraemia, wound infection, endometritis, urinary tract infection (UTI) and pelvic abscess.<sup>8</sup> Because of these issues, early attempts to decrease the incidence of infections with prophylactic antimicrobials were introduced. The overall aim of using prophylactic antimicrobials in caesarean section is to prevent postoperative infection of the surgical site and reduce post operative morbidity and mortality.

Factors that have been associated with an increased risk of infection among women who have a cesarean delivery include emergency cesarean section, labor and its duration, ruptured membranes and the duration of rupture, the socioeconomic status of the woman, number of prenatal visits, vaginal examinations during labour and internal fetal monitoring, UTI, anemia, blood loss, obesity, diabetes, general anesthesia, the skill of the operator and the operative technique.<sup>1,9-12</sup>

The aim of this study was to find the use of antibiotic pattern in caesarean section and to study the frequency of postoperative morbidity and mortality. It is believed that this study would help to develop an antibiotic policy and to decrease the development of antibiotic resistance as well as postoperative mortality and morbidity.

### Materials and Method

This is a prospective cross-sectional study conducted in Prime Medical College Hospital,

Rangpur city from July, 2012 to June, 2013. The study population consisted of women who delivered by cesarean section during that period. Relevant data was collected on a proforma which was prepared according to the protocol designed for the study. The patient related data included age, body weight, parity, socioeconomic status, hospital stay, diagnosis and type of cesarean section (elective or emergency) performed. It also included details of the use of antimicrobial such as choice of antimicrobial, dose, dosage schedule, route of administration and also any change in the antimicrobial following culture and sensitivity. All cesarean sections were done by standard technique. Each patient was examined daily and post-operative infectious morbidity was noted till the date of discharge from the hospital. The following criteria were recognized as infectious morbidity.

**Febrile morbidity:** Oral temperature above 38°C on two or more occasions at four apart excluding first 24 hours after cesarean section.

**Endometritis:** Fever, uterine tenderness and purulent lochia.

**Wound infection:** Cellulitis, fever and exudates.

**UTI:** Fever and positive urine analysis.

Postoperative investigations like pus culture, urine culture, blood culture and antimicrobial sensitivity relevant to the postoperative complications were also recorded. All results were expressed in mean (SD) or percentage as applicable. Statistical analyses were carried out using Statistical Package for Social Science (SPSS) for Windows Version 17.0. Results were considered statistically significant if *p* value less than 0.05.

### Results

The study had a sample size of 356. Patient's demographics and preoperative data are shown in Table 1. Three hundred fourteen patients (88.2%) underwent emergency

caesarean section and 42 patients (11.8%) underwent elective surgery. Regarding socioeconomic condition, 197 (55.3%) patients belonged to lower middle class group, 90 (22.3%) to low socioeconomic group and 69 (19.4%) to upper middle class group. The mean (SD) age of the patients, body weight, parity and haemoglobin concentration was 24.9 (4.8) years, 61.1 (6.3) kg, parity 1.7 (1.2) and 10.0 (1.5) gm/dl, respectively.

Indications of cesarean section are shown in Table 2. Failure to progress labour was the common indication in 121 cases (34.0%)

followed by previous cesarean delivery in 79 cases (22.2%). Usage of antibiotics is shown in Table 3. Most of the patients received ceftriaxone, 209 (58.7%) and cefotaxime, 43 (12.1%). The following two antibiotic combination was administered: ceftriaxone + metronidazole, 37 (10.4%); amoxicillin + clavulanic acid, 31 (8.7%) and cefotaxime + metronidazole, 14 (3.4%). The following three antibiotic combination was administered: ceftriaxone + metronidazole + gentamycin, 11 (3.1%); cefotaxime + metronidazole + gentamycin, 7 (2.0%) and amoxycilline + clavulanic acid + metronidazole, 4 (1.1%).

**Table 1. Patient's demographic and preoperative data, n= 356**

Characteristics	Number	%
Type of cesarean section		
Emergency	314	88.2
Elective	42	11.8
Socioeconomic status		
Lower	90	25.3
Lower middle	197	55.3
Upper middle	69	19.4
Age, years, mean±SD	24.9±4.8	
Body weight, kg, mean±SD	61.1±6.3	
Parity, mean±SD	1.7±1.2	
Haemoglobin concentration, gm/dl, mean±SD	10.0±1.5	

**Table 2. Indications for cesarean section**

Characteristics	Number of cases	%
Failure to progress labour	121	34.0
Previous delivery by cesarean section	79	22.2
Pre-eclampsia	41	11.5
Cephalopelvic disproportion	29	8.1
Bad obstetric history	27	7.6
Foetal distress	23	6.5
Others	36	10.1
Total	356	100.0

**Table 3. Antibiotics used**

Antibiotics	Number of cases	%
Ceftriaxone	209	58.7
Ceftriaxone+Metronidazole	37	10.4
Ceftriaxone+Metronidazole+Gentamycin	11	3.1
Cefotaxime	43	12.1
Cefotaxime +Metronidazole	14	3.9
Cefotaxime +Metronidazole+gentamycin	7	2.0
Amoxicillin+Clavulanic acid	31	8.7
Amoxicillin+Clavulanic acid+Metronidazole	4	1.1
Total	356	100.0

**Table 4. Postoperative infectious morbidity**

Outcome	Number of cases	% out of 55	% out of 356
Febrile morbidity	23	41.8	6.5
Wound infection	15	27.3	4.2
UTI	12	21.8	3.4
Endometritis	5	9.1	1.4
Total	55	100.0	15.5

**Table 5. Duration of antibiotic use and hospital stay in infected and non-infected patients, n = 356**

Variables	Infected patients	Non-infected patients	p value
Duration of antibiotic use, days	12.4±3.5	8.0±2.1	< 0.01
Hospital stay, days	15.4±5.5	9.1±3.9	< 0.01

**Table 6. Isolated micro-organisms in wound infection, UTI and lochia in endometritis**

	Number of cases	% out of 39	% out of 356
Name of organism			
Escherichia coli	16	41.0	4.5
Klebsiella	11	28.2	3.1
Pseudomonas	8	20.5	2.2
Non fermenting gram-negative bacteria	2	5.1	0.6
Enterobacter	1	2.6	0.3
Strepto faecalis	1	2.6	0.3
Total	39	100.0	11.0
Type of infection			
Unimicrobial	25	64.1	7.0
Polymicrobial	14	35.9	3.9
Total	39	100.0	10.9

Postoperative infectious morbidity is shown in Table 4. The overall infectious morbidity was 55 (15.5%) out of 356 patients. Incidence of febrile morbidity, wound infection, UTI and endometritis was found in 23 (6.5%), 15 (4.2%), 12 (3.4%) and endometritis 5 (1.4%) patients. No patients with fever did show any growth in blood culture. Duration of antibiotic use and hospital stay is shown in Table 5. The mean duration (SD) of antibiotic administration was 12.4 (3.5) days in infected patients and 8.0 (2.1) days in non-infected patients, and the difference was statistically significant ( $p < 0.01$ ). The mean duration (SD) of hospital

stay was 15.4 (5.5) and 9.1 (3.9) days for infected and non-infected patients, respectively; and the difference was statistically significant ( $p < 0.01$ ). The micro-organisms isolated from wound infection, UTI and lochia in endometritis are shown in Table 6. The isolated micro-organisms were gram-negative, and Escherichia coli, 16 (41.0%), was the common which was resistant to third generation cephalosporin and sensitive to amikacin; others were Klebsiella 11 (28.2%), pseudomonas 8 (20.5%), non-fermenting gram-negative bacteria 2 (5.1%), enterobacter 1 (2.6%) and strepto faecalis 1 (2.6%). Considering type of infection, 25 cases

(64.1%) had unimicrobial infections and 14 (35.9%) cases had polymicrobial infections.

The isolated micro-organisms were resistant to ceftriaxone and sensitive to amikacin in case of wound infection, resistant to ceftriaxone and ciprofloxacin and sensitive to amikacin in UTI and sensitive to amikacin as well as ciprofloxacin in endometritis. Following the culture sensitivity reports, the patients were given amikacin with the dose of 15 mg/ kg body weight, twice daily intravenously for a period of 7 days and 6 days for wound infection, and UTI and endometritis, respectively.

### Discussion

With all surgical procedure, there is potential for postoperative infection. This is particularly the case for cesarean section, due to the direct anatomical connection of the vagina with the operation site, allowing normal vaginal and bowel flora and pathogens to ascend intra and postoperatively and colonize in both the placental site and the wound site.<sup>13</sup> In surgical practice, there is considerable variation in the timing of prophylactic administration of antimicrobials. Classen et al have shown that timing of antibiotic administration was critical in preventing postoperative wound infections.<sup>14</sup> In all other surgical procedures, administration of prophylactic antibiotics 60 minutes prior to skin incision is a standard to ensure blood levels of antibiotic are optimal at the time of surgery, resulting in less exposure to pathogens and discontinued within 24 hours of surgery.<sup>15</sup>

In this study, mean (SD) age of the patients was 24.9 (4.8) years. Most of the cases were of emergency, because trial labor was tried before taking any patient for surgery, unless there was an absolute indication. Patients with premature rupture of membranes as an indication for cesarean section presented with postoperative complications. This could be due to entry of the vaginal flora to the site of incision. A study conducted on patients undergoing cesarean section also showed premature rupture of membranes as one of the risk factor for the development of postoperative infections.<sup>16</sup> There are similar

studies which demonstrated that women in labor prior to the procedure are at more risk for postoperative complications than those who are not in labor before the time of cesarean section.<sup>17</sup>

In this study, most of the patients were of lower middle class socioeconomic status, the reason being that the study was conducted in the facilities situated in urban area. Studies have shown that patients undergoing cesarean section have a 10% to 85% risk of postoperative infections depending on their socioeconomic status.<sup>18</sup> Increase in postoperative complications in these patients can be due to poor nutritional status. The mean (SD) Hb% of these patients was 10.0 (1.5), this shows that most of the patients were not anaemic; however, anaemia is one of the risk factors for postoperative complications.<sup>16</sup>

In this study, the used antibiotics were of broad-spectrum and most used one was ceftriaxone, a 3<sup>rd</sup> generation cephalosporine and others were combinations of antibiotics. Where antibiotics are used rationally, the Cochrane Database of Systematic Reviews, the American College of Obstetrics and Gynecologists and the Centre for Disease Control and Prevention recommend narrow-range first generation cephalosporins, like cefazolin, to be administered after umbilical cord-clamping for prophylaxis against post cesarean delivery infections.<sup>19,20</sup> In that situation, this may be considered equally effective and less costly than broad-spectrum antibiotics.<sup>21,22</sup> However, due to antibiotic resistance concern, the broad-spectrum antibiotics have been evaluated in this study are mainly single agent extended spectrum penicillins, or 2<sup>nd</sup> or 3<sup>rd</sup> generation cephalosporins.<sup>22</sup> Clinical trials suggest that such extended-spectrum regimens (i.e., a regimen involving the use of both the standard narrow-spectrum antibiotic in addition to a second antibiotic of a different class e.g. azithromycin, gentamycin or metronidazole) are significantly more effective in reducing of post cesarean infections (by 30-60%), hospital stay and costs than the use of narrow-spectrum agents alone.<sup>23-26</sup>

Mean duration of antibiotic use in non-infected patient was about 8 days and infected patient was 12 days. All the patients received antimicrobials intravenously for the first three postoperative days. This is to achieve high and quick plasma concentration of the drug during the period at which the risk of bacterial contamination is more. Patients were then changed to oral formulations for better compliance and cost-effectiveness. In developed countries, prophylactic antibiotics are not used for more than 24 hours because studies have proved that prophylaxis is more efficacious when given in preoperative period and is maintained during surgery and there is no added benefit from multiple dose prophylaxis given after wound closure.<sup>27,28</sup> In developing countries like Bangladesh, prolonged antibiotic therapy is still used considering that facilities for operation theatre sterilization are not ideal.<sup>29</sup> It is expected that prolonged antibiotic therapy will be more effective to control infectious morbidity, although this results in economic burden on health system as well as emergence of resistant organisms.<sup>30,31</sup>

Short term administration of antimicrobials i.e. three perioperative doses is as effective as long term administration in surgical prophylaxis.<sup>32</sup> In a report describing emergence of resistance to antimicrobials, it was found that resistance developed in patients who were continued with antimicrobials for 4 days postoperatively as compared to patients who received only three perioperative doses.<sup>32</sup> This showed that shorter course of prophylactic antimicrobials decreased the emergence of antimicrobial resistance. When patients are administered antimicrobials for a long postoperatively, there may increase cost, which includes acquisition cost and costs for treating postoperative infections related to prophylactic failures due to development of resistance.

Fever was observed in 23 (6.5%) of patients and no organisms were isolated in blood culture. The first spike in temperature appeared on the third postoperative day and subsided by the sixth day. Fever may occur

after any surgical procedure and cesarean section may not necessarily be a marker of infection.<sup>33</sup> It is reported in the present study that the percent of surgical site wound infection of cesarean section was 15 (4.2%), UTI found 12 (3.4%), patients with endometritis 5 (1.4%). The overall infectious morbidity was 55 (16.5%), the incidences of post cesarean infections were similar when compared with other studies.<sup>34,35</sup>

*Escherichia coli* is a commensal of the normal vaginal flora. It was the most common organism isolated in wound infection and UTI in this study. Isolation of bacteria usually not present in the genital tract such as *Pseudomonas* found in the hospital environment and *Acinetobacter* found in the skin shows the iatrogenic aetiology of wound infection. These can be reduced by decreasing the duration of hospital stay and by practicing more strict aseptic measures. Most of the gram-negative organisms isolated in wound infection and UTI were resistant to ceftriaxone and sensitive to amikacin. Gram-positive organisms were sensitive to ciprofloxacin.

This study showed that patients with postoperative infection were hospitalized for about two weeks and non-infected patients stayed one week and the difference was statistically significant. In those instances, patients presented with postoperative infections and failed to improve with antimicrobials; after culture sensitivity antibiotic to which the organism found susceptible was administered. Clarke et al<sup>36</sup> reported that postoperative infection added 8 days to the duration of hospitalization. Other studies also proved that a significant increase in hospital stay occurs when a patient acquires wound infection.<sup>37-39</sup> Increased duration of stay in the hospital can also lead to nosocomial infections which further increase morbidity and mortality.

#### *Conclusion*

All women who underwent cesarean section should receive prophylactic antibiotic. Obstetricians should utilize antibiotic regimens that

are clinically effective and cost-effective. Whenever possible, single agent rather than combination therapy should be used if evidenced clinical efficacy and safety are demonstrated. In all hospitals there is a need for careful surveillance of antibiotic use to prevent emergence of drug resistant strains of bacteria.

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**Suggestion for citation of the above:**

Nazrina S, Chisty S, Maruf AA. Antibiotic prescribing pattern in cesarean section. *Mediscope* 2016;3(1):8-15.