Original Article

Comparative Study of Single Dose Ceftriaxone for Elective Caesarean Section Before Skin Incision and After Cord Clamping in Preventing Post-Operative Infectious Morbidity: A Randomised Controlled Trial

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ABSTRACT

Introduction: The risk of infection is five to twenty times higher for women having caesarean sections than for vaginal deliveries. The routine administration of prophylactic antibiotics lowers the risk of post-caesarean infections by over 50% from baseline rates. Therefore, antibiotic prophylaxis is advised for all women awaiting caesarean sections. Infection and fever complicate caesarean sections in at least 10% and over 15% of cases, respectively, despite the current recommendations for antibiotic prophylaxis procedures. Currently, there is a lack of strong evidence that could recommend the timing of antibiotic prophylaxis in caesarean section.

Aims/ objective: To compare the post-operative infectious morbidity and neonatal outcomes between women receiving ceftriaxone before skin incision or after cord clamping.

Materials and Method: 100 women planned for elective caesarean sections were randomised into two groups BSI and ACC. Women in group BSI were given single dose ceftriaxone 1 gram through intravenous route before 30 – 60 minutes of skin incision. Women in group ACC were given same dose of ceftriaxone through intravenous route just after cord-clamping. Post-operative infectious morbidity such as pyrexia and incidence of surgical site infection and neonatal outcomes such as neonatal sepsis and requirement of resuscitation was compared between two groups.

Results: There was a smaller number of cases with pyrexia in women who were given ceftriaxone before skin incision with the difference being statistically significant ($p< 0.05$). There was also less incidence of purulent discharge, surgical site infection and urinary tract infection in women who were given ceftriaxone before skin incision but the difference was not statistically significant ($p>0.05$). However, there was no statistically significant difference between two groups with respect to any neonatal outcome such as neonatal sepsis and requirement of resuscitation.

Conclusion: Administration of ceftriaxone before skin incision had resulted in slight decrease in infectious morbidity after caesarean section as compared to the administration of the antibiotic after cord clamping. The establishment of enough evidence on the use of antibiotic before caesarean section would promote this intervention resulting in reduction in post-operative maternal and infectious morbidity.

Keywords: Caesarean section, Ceftriaxone, Antibiotic Prophylaxis, Surgical Site Infection, Neonatal outcomes.

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INTRODUCTION

Caesarean section can be described as a delivery method that involves making an incision in both the uterine and lower abdominal walls. It is a highly prevalent and essential surgical treatment carried out to preserve a patient's and her new-born's lives. Every year, more and more babies are delivered via caesarean section. Evidently, it will also lead to an increase in complications from surgery. [1] Following caesarean procedure, infectious morbidities are a major cause of complications and carry a high mortality risk. [2] The administration of antibiotics to avoid postoperative infection problems is known as antibiotic prophylaxis. It is possible for it to be primary, secondary (suppression), or eradicating. [3] Previous studies have demonstrated that pre-C-section antibiotic treatment can reduce the risk of postoperative infection problems. Numerous medications are readily available and can significantly lower the incidence of surgical wound infection. [4]

The risk of infection is five to twenty times higher for women having caesarean sections than for vaginal deliveries. 5 The routine administration of prophylactic antibiotics lowers the risk of post-caesarean infections by over 50% from baseline rates, which are as much as 20-50%. 5 Therefore, antibiotic prophylaxis is advised for all women awaiting caesarean sections. [5] Infection and fever complicate caesarean sections in at least 10% and over 15% of cases, respectively, despite the current recommendations for antibiotic prophylaxis procedures. [5]

Fever, bacterial infection of the wound, endometritis, bacteraemia, various serious infections such as pelvic abscess, septic shock, necrotizing fasciitis, and septic pelvic vein thrombophlebitis, and urinary tract infection (UTI) are among the infectious problems that can arise after a caesarean section. [6]

The misuse of antibiotics is the primary cause of the development of antibiotic resistance. Unnecessary usage of broader spectrum regimens and incomplete antibiotic therapy courses are factors. [7] Most practitioners continue to favour prolonged antibiotic coverage. Antibiotic prophylaxis refers to the use of antibiotics to stop the spread of infection, whereas antibiotic therapy refers to the use of antibiotics to treat an existing infection. [8] Prophylactic antibiotic use serves as a supplement to reduce intraoperative microbial burden to a level that can be controlled by the host's innate and adaptive immune responses, not to sterilise tissue. [9-11]

To reach adequate tissue levels of antibiotics at the moment of microbial infection is the aim of antibiotic therapy. [8] An antibiotic regimen (for prophylaxis) should ideally have been demonstrated to be effective in well-designed prospective, randomised, double-blind clinical trials, be active against a wide range of pathogens probably to be involved, achieve sufficient serum and tissue levels during the procedure, not be linked to the emergence of antibiotic resistance, be reasonably priced, and be well-tolerated.

Both penicillin and cephalosporins meet these requirements in many ways. [12] Currently, the ACOG and CDG recommend limited range, one dose of 1st generation cephalosporin prophylaxis in the Cochrane database of systemic reviews due to the fact that these remove contaminants during surgery effectively. [6]

In a 2014 Cochrane study, which compared antibiotic prophylaxis with no prophylaxis, it was shown that prophylaxis with antibiotics reduced the incidence of endometritis, postoperative infections of wounds, and severe infectious sequelae by 60–70%. [13] However, in obstetrics, antibiotics are given after cord clamping because there is a theoretical worry that providing antibiotics to the foetus could disguise a new-born infection. [14] As a result, preventive antibiotics have frequently been postponed until after surgical birth and new-born umbilical cord clamping. As an example, a 1999 recommendation from the Centre for Disease Control and Prevention in Atlanta (USA) recommended antibiotic use only in vulnerable caesarean deliveries. [15]

In order to prevent or lower the risk of maternal infections following the surgical operation, prophylactic antibiotics were recommended in several guidelines and evaluations from 2008 to be administered before cord clamping. [16-19]

Currently, there is a lack of strong evidence that could recommend the timing of antibiotic prophylaxis in caesarean section. Thus, this study was planned to compare the post-operative infectious morbidity and neonatal outcomes between women receiving ceftriaxone before skin incision or after cord clamping.

MATERIALS AND METHODS

This was an open label randomised controlled trial with parallel 1:1 allocation carried out in the Department Obstetrics and Gynaecology of tertiary care centre of eastern India from August 2021 to July 2022. The study was carried out according to principles of good clinical practice and declaration of Helsinki. The study participants to be enrolled were given participant information sheet and it was explained to them, thereafter written informed consent was taken from them.

Inclusion Criteria: Women planned for delivery through elective lower segment caesarean section in the study period.

Exclusion criteria: Women having history of diabetes mellitus, obese women having BMI greater than or equal to 25, women with premature rupture of membranes, HIV positive women, women on immunosuppressive drugs, women who received any antibiotics within 14 days of surgery or women having history of hypersensitivity reaction to cephalosporins were excluded from study.

100 women planned for elective caesarean sections were randomised into two groups BSI and ACC. The randomisation was done using web-generated random numbers. Women in group BSI were given single dose ceftriaxone 1 gram through intravenous route before 30 – 60 minutes of skin incision. Women in group ACC were given same dose of ceftriaxone through intravenous route just after cord-clamping.

Age, parity, gestational age, indication for elective caesarean section, postoperative complications like endometritis and pyrexia, surgical site infection, urinary tract infection, and other serious infectious morbidities like bacteraemia, septic shock, septic thrombophlebitis, necrotizing fasciitis, or infection-related death were among the variables examined. When uterine discomfort, foul-smelling lochia, tachycardia, leucocytosis, and a maternal temperature of more than 100.4 F were present on two different occasions, endometritis was determined to be the cause. Purulent discharge, erythema, and induration of the surgical site were signs of surgical site infections. Maternal fever, flank pain, and a urine culture showing more than 105 colonies of gram-negative urinary pathogens are used to diagnosis urinary tract infection.

Neonatal outcomes evaluated included neonatal sepsis identified by positive blood culture, requirement of neonatal resuscitation, NICU hospitalisation, as well as the immediate harmful effects of drugs on the infant including uncontrollable diarrhoea and rashes.

Statistical Analysis

Data collected from study participants were presented in tabular form using Microsoft Excel 365 and then transferred to graph pad prism version 8.4.3 Data were in

mean ± SD (standard deviation) continuous variables such as age, haemoglobin, duration of surgery and using frequency and percentage for categorical data such as maternal and neonatal outcomes. Unpaired t test and fisher's exact test were used to determine statistical significance of difference between two groups in continuous and categorical variables respectively. The two-tailed p value of less 0.05 was taken as measure of statistical significance.

OBSERVATIONS AND RESULTS

Table 1: Comparison of baseline demographic and clinical parameters between the two groups

Parameters	Group BSI (n = 50)	Group ACC (n = 50)	P-Value
Age in years (Mean ± SD)	27.54 ± 3.48	27.02 ± 2.41	0.39*
Number of primigravida	23	21	0.84**
Gestation age years (Mean ± SD)	39.24 ± 1.08	38.87 ± 1.15	0.10*
Haemoglobin in g/dl (Mean ± SD)	10.32 ± 1.53	10.71 ± 1.78	0.24*
Duration of surgery in minutes (Mean ± SD)	61.72 ± 11.43	60.95 ± 12.06	0.74*
*Unpaired t-test **Fisher's exact test			

Both the groups were comparable with respect to age, parity, gestational age, haemoglobin, and duration of surgery with no statistically significant difference in these parameters (p >0.05).

Table 2: Comparison of maternal outcome between two groups

Parameters	Group BSI (n = 50)	Group ACC (n = 50)	P-Value (Fisher's exact test)
Pyrexia	5	14	0.04
Superficial SSI with induration and erythema	4	6	0.74
Purulent discharge	6	11	0.29
Serosanguinous discharge	3	6	0.49
Deep incisional SSI	0	1	>0.999
Endometritis	0	0	>0.999
Urinary Tract Infection	5	11	0.17
SSI: Surgical Site Infection			

There was a smaller number of cases with pyrexia in women who were given ceftriaxone before skin incision with the difference being statistically significant (p< 0.05). There was also less incidence of purulent discharge, surgical site infection and urinary tract infection in women who were given ceftriaxone before skin incision but the difference was not statistically significant (p>0.05). There was no case of endometritis in either group.

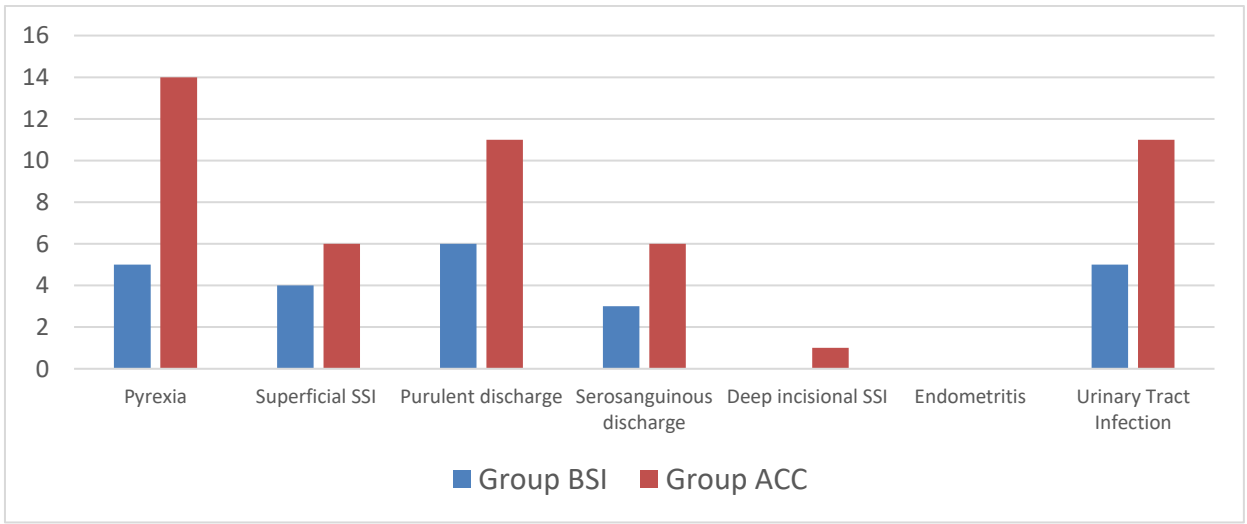

Figure 1: Comparison of Maternal Outcomes between Two Groups

Table 3: Comparison of neonatal outcome between two groups

Parameters	Group BSI (n = 50)	Group ACC (n = 50)	P-Value (Fisher's exact test)
Requirement of resuscitation	6	4	0.74
NICU admission	8	9	>0.999
Respiratory distress	5	6	
Neonatal sepsis	1	2	
Anomaly	0	0	

Proportion of new-borns who required resuscitation or NICU admission was slightly greater and incidence of neonatal sepsis was less in women who were given ceftriaxone before skin incision. However, there was no statistically significant difference between two groups with respect to any neonatal outcome.

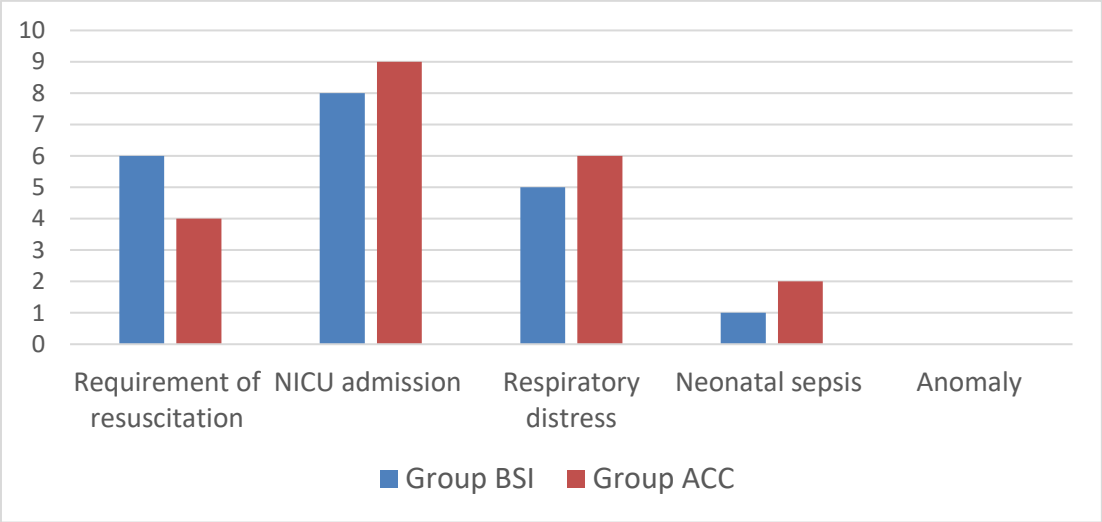

Figure 2: Comparison of Neonatal Outcomes between Two Groups

DISCUSSION

One of the most common medical procedures worldwide is a caesarean section. The majority of post-operative problems are infectious morbidities including endometritis and surgical site infection. Antibiotic prophylaxis has been shown to reduce infectious morbidity in both high-risk and low-risk women who have elective caesarean sections. Only low risk women without conditions such severe anaemia, obesity, or diabetes mellitus were included in our study. To avoid the bias of many factors involved in emergency caesarean sections, only elective caesarean sections were taken into consideration. An elective caesarean section is one that is performed on a woman with intact membranes before the start of labour.

In the current research, ceftriaxone was chosen because it is highly stable in the presence of beta-lactamases, penicillinases, and cephalosporinases, and it is efficient against both gram-negative and gram-positive bacteria. There is lack of clear and strong evidence regarding the timing of the antibiotic prophylaxis. The customary procedure has been to only deliver one medication—typically a cephalosporin—during cord clamping in an effort to protect the unborn child from exposure to drugs that could conceal infection of new-born. According to some studies, giving antibiotics 15–30 minutes before making a skin incision reduces infectious morbidity without having an impact on the outcome for the new-born. [14, 20-22]

According to previous studies, having a caesarean section increases the chance of infection by 5 to 20 times compared to giving birth vaginally, making it the single most significant risk factor for postpartum infection. [5] Pre-incision cefazolin use resulted in 50% reduction in overall incidence of infection, a 53% reduction in incidence of endometritis, and a statistically significant 40 percent decrease in incidence of surgical site infection when compared to administration of ame drug after cord clamping, according to a meta-analysis that included three randomised controlled trials with an average sample size of 749. [14]

In the current study, it was discovered that women who received ceftriaxone prior to skin incision had about 50% lower chance of surgical site wound infection than women who received it following cord clamping. But statistical significance was not seen in this. In the current investigation, there were no cases of endometritis. In a double-blinded randomised controlled experiment by Thigpen et al., which included 302 women as participants, the cord clamping group experienced higher endometritis cases (14,7%) than the skin incision group (7.8%). Infection rates for surgical site were 3.9% for skin incision group and 5.4% for cord clamping group. The rates of post-infectious

morbidity did not differ between the two groups, according to their findings. [23]

Owens et al. found that the administration of prophylactic antibiotics before skin incision, compared with after cord clamping, was associated with a forty percent decrease in postpartum endometritis (3.9-2.2%) and a thirty percent decrease in surgical site infection (3.6-2.5%) with a sample size of 9,010 women (4,781 women in group 1 were given antibiotic prior to skin incision and 4,229 women in group 2 were given following cord clamping). 22 Endometritis developed in roughly 5% of group 2 compared to 1% of group 1 in Sullivan et al.'s randomised controlled trial, which included 357 women (175 women in group 1 who were given cefazolin before the skin incision and 182 women in group 2 who were given the same drug following cord clamping). [21] In their study, 5% of those in group 2 developed surgical site infections, compared to 3% of those in group 1. [21] The group that received the antibiotics prior to skin incision experienced considerably lower rates of endometritis and overall post-operative infectious morbidity than the group that received the drug following cord clamping.

In Witt et al.'s randomised controlled trial, which included 1,112 women divided into three group respectively (women of group 1 were given 2 g cefazolin prior to skin incision, women in group 2 were given the same following cord clamping, and women group 3 were given saline infusion before skin incision), approximately 2.4% of the women in groups 1 and 2 experienced surgical site infection, and approximately 0.3% of the women in groups 1 and 2 experienced endometritis.[24] Urinary tract infection affected 1.1% and 2.2% of the females in groups 1 and 2, respectively. In the majority of the trials, there was no statistically significant difference between the two groups, with the exception of Sullivan et al. and Owens et al., where the risk of surgical site infections was decreased when the antibiotics were given prior to skin incision as opposed to following cord clamping. However, both elective and emergency caesarean sections were included in these researches. [21, 22]

None of the women in the study's two groups experienced endometritis. In our research, routine cervical swab cultures were not performed. Our hospital's policy is to only perform cervical swab cultures when fever is accompanied by pungent-smelling lochia and pain in the uterus.

In the current study, women who received ceftriaxone prior to skin incision had a lower incidence of fever. Fever occurred in 7% of women in Alekwe et al.'s study, which compared the efficiency of single dose ceftriaxone with numerous doses of antibiotics in avoiding post-caesarean infectious morbidity. [25] Fever occurred in 20 patients (8.3%) in the study by Bagratee et al., which examined whether prophylactic antibiotics given at the point of an elective caesarean delivery minimise post-caesarean infectious morbidity. [26]

In our study, 5 women in the BSI group and 7 women in the ACC group developed urinary tract infections. The likely causes could be that standard catheterization during the surgery may have exacerbated the infection and that not all the women were checked for asymptomatic bacteriuria during prenatal screening. On the first post-operative day after the catheter has been withdrawn, it should be hospital protocol for all patients to undergo a urine culture.

Approximately 16% of the neonates in both groups in the current study required NICU admission, which was higher than in earlier studies. [21, 23] Admission was required due to respiratory distress, premature birth, etc. Neonatal sepsis involving a positive blood culture affected roughly 2% of neonates of the women receiving ceftriaxone before skin incision and 1.8% of new-borns of the women receiving the drug after cord clamping in the current study. The results of Owens et al. and this finding is comparable. [22] Overall, new-born infections or NICU hospitalisation were unaffected by antibiotic prophylaxis prior to skin incision.

Our study had the drawback that none of the women who participated were at high risk for post-caesarean infectious morbidities. On the fourth post-operative day, each study participant was examined for infections; if none were found, the majority were released. Late infections were not assessed as a result. Because all pregnant women were not routinely evaluated for asymptomatic bacteriuria throughout the prenatal period, there may have been a higher frequency of urinary tract infections with positive cultures.

CONCLUSION

Administration of ceftriaxone before skin incision had resulted in slight decrease in infectious morbidity after caesarean section as compared to the administration of the antibiotic after cord clamping. There were no significant changes in adverse neonatal outcome on giving the antibiotic before skin incision, therefore our study result suggests further research on testing the theoretical concern about risk of adverse neonatal outcome associated with administration of the antibiotic before surgery. The establishment of enough evidence on the use of antibiotic before caesarean section would promote this intervention resulting in reduction in post-operative maternal and infectious morbidity.

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