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## Original Research Article

# A prospective randomised clinical trial of prophylactic antibiotic in caesarean delivery and fetomaternal outcome

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### ABSTRACT

**Background:** Infectious maternal and perinatal morbidities are 5 to 20 times more in caesarean section when compared to vaginal births. Objective of present study was to assess the rates of maternal and neonatal infectious morbidities following administration of antibiotic before skin incision compared to given after umbilical cord clamping during caesarean delivery.

**Methods:** 185 pregnant women with gestational periods more than 34 weeks who were prepared for caesarean delivery, randomized to single dose antibiotic given either before skin incision (study group) or after umbilical cord clamping (control group). Primary outcome measures: maternal postoperative infections morbidities. Secondary outcome measures: neonatal infections morbidities with Sick Newborn Care Unit (SNCU) admissions and postoperative hospital stay of mother.

**Results:** Surgical Site Infections (SSI) and postoperative fever were significantly less in the study group than the control group so also the lesser incidences of endometritis but no statistically significant difference in the incidence of peritonitis and wound dehiscence were observed in both groups. No significant differences were seen in neonatal infectious morbidities and SNCU admission when compared in both groups. There was significantly less mean postoperative hospital stay of mothers in the group who received prophylactic antibiotic pre-incision.

**Conclusions:** Antibiotic given 30-60 minutes before skin incision significantly decreases maternal postoperative infectious morbidities barring neonate.

**Keywords:** Caesarean delivery, Postoperative, Prophylactic antibiotic, Surgical site infections

### INTRODUCTION

Infectious maternal and perinatal morbidities are 5 to 20 times more in caesarean section when compared to vaginal births.<sup>1</sup>

Genital tract is most important source of infections particularly when membrane is ruptured and also even if membranes are intact, polymicrobial invasion of intrauterine cavity occurs especially with preterm labour.<sup>2</sup> The purpose of prophylactic antibiotic in surgeries is not

for sterilisation of tissue but for reducing colonization of microorganisms introduced during operation to a level to overcome by patient's immunity.<sup>3</sup> Broad spectrum antibiotic like cephalosporins are most commonly administered for SSI prophylaxis.<sup>4</sup> The dosage should be adequate to exceed minimum inhibitory concentration (MIC) for the organism likely to be encountered during the operation. Prophylactic antibiotic during caesarean delivery has usually been given after umbilical cord clamping for apprehension of fetal exposure through placenta if administered earlier.

However recent studies involving pregnant women including research in nonpregnant populations undergoing operations have suggested that antibiotics given before incision (ideally 30-60 minutes) to allow for optimal concentration at the surgical site reduce SSI by almost half compared to administration during operation or after cord clamping and there is no increase in adverse neonatal outcome.<sup>5-8</sup>

So, a prospective randomized clinical trial was undertaken to notice whether prophylactic antibiotic given before skin incision than after cord clamping, was more effective for preventing infectious morbidities of mother and newborn baby following caesarean delivery.

## METHODS

This prospective randomised study was done at antenatal ward and labour Operation theatre in the department of Obstetrics and Gynaecology, Nilratan Sircar Medical College and Hospital, Kolkata India for the period from April, 2015 to March, 2016. Pregnant women of more than 34 weeks of gestational age admitted in labour and fulfilling eligibility criteria and giving consent were subjected to our study as prematurity is an independent risk for adverse perinatal outcome.

A total of 185 women were randomized after going through exclusion criteria among 200 women as follows:

- patients who are febrile during or prior to screening,
- ruptured membranes more than equal to 18 hrs with or without antibiotic prophylaxis
- patients with chronic diseases like diabetes mellitus, heart disease, renal disease etc.
- patients who have received antibiotics within one week prior to caesarean section for other reasons,
- patients with obstetrics complications like pre-eclampsia, antepartum haemorrhage, or indications for emergency caesarean deliveries like obstructed labour, deep transverse arrest, fetal distress etc,
- penicillin or cephalosporin allergy. Those women who were in stable condition enough to delay caesarean section for 90 minutes to 120 minutes in situations like cephalo pelvic disproportion, intrauterine growth retardation with oligohydramnios, malpresentation detected early in labour, were also included in the study.

In present study 200 pregnant women above 34 weeks of gestation admitted in antenatal ward taking clearance from institutional Ethical Committee of NRS Medical College and proper consent were taken from patients. After enrolment, a detailed history regarding age, parity, sociodemographic conditions, period of gestations were taken. Detailed past and present menstrual, medical, surgical and obstetrical histories were also taken. Then thorough general and obstetric examinations were done. 9 women were excluded who not meeting inclusion criteria and 6 women were refused to participate. Ultimately 185

women were randomized fulfilling inclusion and exclusion criteria as before and were allocated into two groups: Group A is study group comprising 92 subjects having given ceftriaxone injection 1 gram intravenously 30-60 minutes before skin incision after a test done of 100mg intradermal ceftriaxone given slowly over 10 minutes and Group B is the control group comprising 93 subjects having given antibiotic in the same dosage after cord clamping. None of the subjects were lost to follow up and 92 subjects were analyzed in the study group and 93 subjects were analyzed in control group.

The sample size was calculated using previous hospital records of our institution taking 15% difference in observation of proportions of using prophylactic antibiotics before caesarean delivery having alpha-error as 0.05 (i.e. 1.96) and beta error at power of 80 (i.e. 0.84) resulting minimum members of 77 subjects in each group; thus, validating our present study with adequate member of subjects in the study and control groups.

Standard technique of caesarean section was followed having pfannenstiel skin incision, two layer closure of uterine wound and non stitching of peritoneum were done by visiting surgeons, RMOs and SRs assisted by JRs. Post operative follow up done for signs of SSI, fever, endometritis, neonatal sepsis, SNCU admission and hospital stay of mother. SSI were diagnosed if there is purulent discharge, erythema and induration of incision site; hematomas, seromas or wound breakdown in the absence of previously described signs were not included. Fever was diagnosed when temperature was more than 100.4°F on two occasions 6 hrs apart, excluding first 24 hrs of delivery. Endometritis was elicited if there is presence of fever with lower abdominal or uterine tenderness with tachycardia, leucocytosis, subinvolution of uterus and foul smelling lochia. High vaginal swab may or may not be positive for organisms. Peritonitis presents as fever, abdominal pain, muscle guarding, rebound tenderness, sinus tachycardia, ileus paralyticus, leucocytosis and abscess in peritoneal cavity. Neonatal sepsis was diagnosed by clinical examination, blood picture, C-reactive protein and positive blood culture as appropriate determined by neonatologist.

Primary outcome measures were postoperative infectious morbidities of mother and secondary outcome measures were neonatal sepsis, SNCU admissions of babies and postoperative hospital stay of mothers.

## Statistical analysis

All clinical and operative observations were recorded by researchers using Microsoft Excel and collected data were analysed by statistical methods, using Quick Calcs, socscistatistics.com having Easy Fisher Exact Test Calculator etc. A P- value less than 0.05 having 95% confidence interval was considered statistically significant. Normality of data has been tested by Shapiro-Wilk test. Unpaired t-test has been used to find the

significance of study parameters between two groups. Chi-square test/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two groups.

## RESULTS

Out of 200 pregnant women enrolled for assessments of eligibility, 15 women were excluded from the study due to either not meeting the inclusion criteria (n=9) or refrained to participate (n=6). So, 185 women were randomized into two groups; 92 in study group (group A) and 93 in the control group (group B). Prophylactic antibiotic (Inj. Ceftriaxone 1 gram i.v.) was injected 30-60 minutes prior to skin incision during caesarean delivery in group A and after umbilical cord clamping in group B. No subject was lost to follow-up and hence all women analyzed according to the intention-to-treat protocol.

**Table 1: Demographic characteristics.**

Characteristics	Study group (n=92)	Control Group (n=93)	P-value (95% CI)
Age in years (mean±SD)	24.32±3.01 (t=0.1327, df=183, SE=0.452)	24.26±3.14	0.8946* (-0.8324 to 0.9524)
BMI (mean±SD)	24.81±2.15 (t=1.2107, df=183, SE=0.322)	25.20±2.23	0.2276* (-0.0255 to 0.2455)
Gestational age in weeks (mean±SD)	37.62±1.54 (t=1.2823, df=183, SE=0.234)	37.92±1.64	0.2014* (-0.7616 to 0.1616)
<b>Indications for LSCS</b>			
Emergency	52(56.52%)	58(62.37%)	0.0822**
Elective	40(43.48%)	35(37.63%)	0.0843**

\*P-value (two tailed); \*\* Mid-P exact; SD: Standard Deviation; BMI: Body Mass Index; LSCS: Lower Segment Caesarean Section; CI: Confidence Interval.

Demographic characteristics of women in both groups were identical as shown in Table 1 in relation to age (24.32±3.01 vs 24.26±3.14, P=0.8946, 95% CI= -0.8324 to 0.9524), BMI (24.81±2.15 vs 25.20±2.23, P=0.2276, 95% CI=-0.0255 to 0.2455), gestational age in weeks (37.62±1.54 vs 37.92±1.64, P=0.2014, 95% CI= -0.7616 to 0.1616) and indication of caesarean deliveries also and they are statistically not significant (p>0.05).

In Table 2 the prospective maternal infections morbidities showed statistically significant difference in between the two groups with respect to fever from 2nd post operative day (5.43% vs 21.50 %, P=0.020), SSI (3.26% vs 8.60%, P=0.0039) and endometritis (5.26% vs 19.35%, P=0.00075%) but not significant when wound dehiscence (1.08% vs 2.15%, P=0.0657) and peritonitis (1.085 vs 3.22%, P=0.0694) were considered.

**Table 2: Postoperative maternal infectious morbidities.**

Outcome	Study group (n=92)	Control group (n=93)	P-value*
Fever (From 2nd post-operative day)	5 (5.43%)	20 (21.50%)	0.0020
SSI	9 (3.26%)	25 (8.60%)	0.0039
Wound dehiscence	1 (1.08%)	2 (2.15%)	0.0657
Endometriosis	3 (3.26%)	18 (19.35%)	0.0007
Peritonitis	1 (1.08%)	3 (3.22%)	0.0694

Mid-P exact; SSI: Surgical Site Infection

There was no significant difference in neonatal outcomes as shown in table 3 when the following parameters were taken into account like sepsis, fever, poor feeding, birth asphyxia, SNCU admissions; as P=>0.05 between the groups. But mean postoperative study of mothers in hospital was statistically significant by less in the study group than the control group (5.05=-1.67 vs 7.11=-1.55, P=0.0001, 95% CI= -2.4756 to -1.6444).

**Table 3: Neonatal infectious morbidities, SNCU admissions and postoperative hospital stay of mother.**

outcome	Study group (n=92),	Control group (n=93)	Pvalue
Sepsis	3 (3.26%)	5 (5.37%)	0.0693*
Fever	2 (2.17%)	3 (3.22%)	0.0656*
Poor feeding	3 (3.26%)	4 (4.30%)	0.0655*
Birth asphyxia	1 (1.08%)	1 (1.07%)	0.0620*
SNCU admission	6 (6.52%)	10 (10.75%)	0.0766*
Post-operative hospital stay of mother (mean±SD)	5.05±1.67 (t=9.7805, df=183, SE=0.211)	7.11±1.15	0.0001** (-2.4756 to -1.6444)

\*denotes Mid-P exact and \*\*denotes P-value (two tailed).

## DISCUSSION

Both elective and emergency caesarean deliveries are benefited when prophylactic antibiotic is used - long acting, less costly and having fewer side effects is preferred.

A cephalosporin namely ceftriaxone is chosen for effective prophylaxis against post operative infection morbidities following caesarean sections in many previous clinical trials.<sup>9-11</sup> Present study determines the difference of infectious morbidities in mothers and neonates between pre operative use of prophylactic antibiotic and the use after cord-clamping during caesarean delivery.

The demographic characteristics were comparable in two groups with no significant differences in relation to mean age in years (P=0.8946; 95% CI of -0.8324 to 0.9524), BMI (P=0.2276; 95% CI of -0.7616 to 0.1616). These results are consistent with the results of studies conducted

previously by Thigpen et al, Sullivan et al, Bhattacharjee N et al and also Alakananda et al.<sup>12-15</sup> There was also no statistically significant difference between groups found in indication for LSCS in emergency ( $P=0.0822$ ) and elective ( $P=0.0813$ ). Similar study was done by Thigpen et al previously showing no significant differences in indication for LSCS ( $P=0.54$ ).<sup>12</sup>

In present study only 5.43% of patients developed fever from 2<sup>nd</sup> postoperative day onwards in the study group than in the control group where it was 21.5% showing a significant difference ( $P=0.0020$ ). In the study conducted by Bhattacharya et al, 33% of the patients who received antibiotic after cord clamping had more postoperative fever than in 26% of the patient with fever who received antibiotic before skin incision.<sup>14</sup> Baaqeel et al found that there was nonsignificant reduction in maternal febrile morbidity in group who received preoperative antibiotic.<sup>16</sup> Smaill FM et al conducted RCT found that there was decreased incidence of maternal febrile morbidity in the group who received pre operative antibiotic.<sup>17</sup>

In study conducted by Kalarnjini S et al no significant difference in fever was found. In present study complications like SSI in terms of induration, erythema and wound discharge were seen in 3.26% in study group and 8.60% in the control group with significant differences ( $P=0.0039$ ).<sup>18</sup> Similar results were found in the studies conducted by Sullivan et al, Kaimal et al, Owens et al, Lamont RF et al, Alakanada et al, but insignificant results were found in studies conducted by Baaqeel et al, Heesen et al, Sun J et al and Zhang C et al.<sup>7,13,15,19-23</sup>

Endometritis was found in 3.26% of the patients in the pre-incision group than 19.35% of the patients in the control group showing statistically significant difference ( $P=0.0007$ ). In the studies conducted by Sullivan et al, Costantine MM et al, Kaimal MD et al, Baaqeel et al, Heesen et al, Bhattacharjee N et al, Sun J et al, Mackeen AD et al, Smaill FM et al; the incidence of postpartum endometritis was reduced in the group who received antibiotic pre-incision as compared to group who received antibiotic after cord clamping.<sup>6,13,14,16,17,19,21,22,24,25</sup> But Thigpen et al and Zhang C proposed no significant difference in postoperative endometritis in both groups.<sup>12,23</sup>

Wound dehiscence occurred insignificantly in both the groups ( $P=0.0657$ ) as well as the incidence of peritonitis ( $P=0.0694$ ). Similar results happened in the study conducted by Bhattacharjee N et al ( $P=0.288$  for wound dehiscence).<sup>14</sup> Young BC et al found that infectious morbidity fell from 5.4% to 2.5% when antibiotic given before skin incision.<sup>26</sup>

Costantine MM et al found decreased rates of total infectious morbidity ( $P=0.15$ ) in the group who received pre incision antibiotic.<sup>6</sup> Brown J et al, Mackeen AD et al, Smaill FM et al, Sullivan et al showed decreased rates of

maternal infectious morbidity in pre incision group.<sup>24,25,27</sup> Witt A et al and Zhang C et al found no significant difference in total infectious morbidity in both groups.<sup>23,28</sup>

Present study revealed neonatal morbidities like neonatal sepsis ( $p=0.0693$ ), neonatal fever ( $P=0.0656$ ), neonatal poor feeding ( $P=0.0655$ ), birth asphyxia (0.0620), SNCU admission ( $P=0.0766$ ) had no significant differences in both group; results were similar in the previous studies also as mentioned in above paragraph. Mean hospital stay of mothers was significantly less in study group ( $P=0.0001$ ) which is consistent with other studies as of Smaill F et al and Bhattacharjee N et al.<sup>14,17</sup>

The sample size was medium but significant. Pharmacokinetics of antibiotic in individual patient could not be compared. Intraoperative and immediate post operative blood loss was not estimated though blood transfusion was not required in any patient in both of the groups

## CONCLUSION

Prophylactic administration of antibiotic at 30-60 minutes before the incision of skin during caesarean section have better maternal outcome when infectious morbidities and postoperative hospital stay were accounted without any difference in neonatal outcome than antibiotic used after umbilical cord clamping after delivery of the baby.

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