Bangladesh J Obstet Gynaecol, 2024; Vol. 39(1): 18-23

Association between Timing of Prophylactic Antibiotic in Cesarean Section and Risk of Postpartum and Neonatal Infections

MST. AFROZA KHANUM[1], MST.NAZMUNNAHER MINA[2], SALMA LOVEREEN[3], S.M. MUNIRUZZAMAN[4], ROMANA[5], MASUDA BEGOM[6]

Abstract:

Objective: *This study aimed to compare postpartum infections and neonatal sepsis in relation to the timing of perioperative antibiotics at cesarean section.*

Material and Methods: *This was a prospective randomized controlled trial in Monno Medical College & Hospital of Manikganj. 176 patients with singleton, live, term or near term pregnancies fulfilling the inclusion and exclusion criteria were included in the study. All the patients underwent caesarean section between June 2014 to May 2015. The population was divided into two groups:*

Group - A (89 Patients) and Group –B (87 Patients). Group A (89) received injectable antibiotic Ceftriaxone 1 gm 30-60 minutes before skin incision and Group –B (87) received the same antibiotic after cord clamping. Rates of postoperative infections, endometritis, UTI, and wound infection(SSI) and neonatal sepsis were compared between two groups.

Results: *There were 176 patients enrolled and no demographic difference were observed between two groups. No significant difference was found between the groups for total infectious morbidity. Rates of endometrities (P=1.0), UTI (P=0.5), Febrile morbidity (P= 0.77), wound infection (SSI) (P=0.4), neonatal sepsis (P=0.77), NICU (P=0.1), NICU length of stay (P=0.67).*

Conclusions: *Time of prophylactic antibiotic application does not change maternal infectious morbidity in cesarean section deliveries, preoperative prophylaxis application does not affect neonate morbidity rate as stated in literature.*

Keywords: *Antibiotic prophylaxis, cesarean section, neonatal sepsis, maternal infection.*

Introduction:

Infection is the most common complication following cesarean section[1]. The risk of postpartum infection seems to be nearly five-fold increased after CS compared with vaginal birth[2]. Infections can affect the pelvic organs, the surgical wound, and the Urinary tract Infectious complications that occur after cesarean births are an important and substantial cause of maternal morbidity and are associated with a significant increase in hospital stay[1].

Over the years; global caesarian section (CS) rates have significantly increased from around 7% in 1990 to 21% today surpassing the ideal acceptable CS rate which is around 10%–15% according to the WHO[3]. Compared with placebo or no treatment, the use of prophylactic antibiotics in women undergoing cesarean section reduced the incidence of wound infection (RR 0.40, 95% CI 0.35 to 0.46, 82 studies, 14,407 women), endometritis (RR 0.38, 95% CI 0.34 to 0.42, 83 studies, 13,548 women) and maternal serious infectious complications (RR 0.31, 95% CI 0.20 to 0.49, 32 studies, 6159 women)[4].

The principles of presurgical administration of antibiotics are well defined, but a few controversies

1. Associate Professor (Obst & Gynae), Monno Medical College & Hospital, Manikganj
2. Associate Professor (Obs & Gynae),Delta Medical College & Hospital, Dhaka, Bangladesh
3. Associate Professor, Department of Gynaecology &Obstetrics, Ibn Sina Medical College, Dhaka, Bangladesh
4. Assistant Professor (Pediatric), Monno Medical College & Hospital, Manikganj
5. Registrar, Monno Medical College & Hospital.
6. Professor (Obst & Gynae), Dhaka Medical College

Address of Correspondence: Dr. Mst. Afroza Khanum. Associate Professor(Obst & Gynae), Monno Medical College & Hospital, Manikganj, e-mail: dr.afrozakhanum63@gmail.com

persist. An ideal antimicrobial agent would not induce bacterial resistance in pathogenic organisms, would penetrate tissues effectively, would have a long enough half-life so that a single injection could guarantee protection throughout the operation, would have a low toxicity, would not interfere with anesthetics, would be easy to administer, and would be cost-effective.[5] The data from a large multicenter collaborative study shows a consistent relationship between the timing of AMP and SSI risk with a trend toward lower risk occurring when AMP were given within 30 minutes prior to incision[6].

Evidence-based guidelines recommend the use of prophylactic antibiotics prior to surgical incision. An exception is made for cesarean delivery, where narrow-range antibiotics are administered post umbilical cord clamping because of putative neonatal benefit. Prophylactic antibiotics in most institutions are administered generally after clamping the umbilical cord[7, 8] as there is an argument to delay antibiotics until after cord camping because relevant antibiotic plasma levels are seen in the neonate[9].

The most important source of microorganisms responsible for post-cesarean section infection is the genital tract, particularly if the membranes are ruptured. Infections are commonly polymicrobial. However inappropriate use of antimicrobials in surgeries can select for resistant micro-organisms [10] and it has been shown to result in marked changes in an individual's skin flora and strains with increased virulence seen postoperatively[11]. There are few randomized controlled studies on the timing of antibiotic prophylaxis in cesarean section. Zhang C et, al[12] concluded that there was no difference in infectious morbidity between pre-operative antibiotics and those given at cord clump. On the other hand, Costantine et, al [13] reported a decrease in both endomyometritis and total post-cesarean infectious morbidity in a prospective randomized trial with the use of preoperative Cefazolin prophylaxis.

This present study aims at comparing the timing of administering perioperative antibiotics in cesarean section i.e. before skin incision and after cord clamping, and assessing risks of postoperative maternal and neonatal infections.

Materials and Methods:

The Ethical Committee of Monno Medical College & Hospital approved this randomized controlled study. Singleton, live, term or near-term patients undergoing elective or emergency cesarean section in the Department of Obstetrics and Gynecology in Monno Medical College & Hospital from June 2014 to May 2015 were included in the study. The exclusion criteria were PROM, PROM, case of DM or GDM, Prolonged labor, Obstructed labor, Suspected chorioamnionitis, cases of UTI, anemia (Hb< 10gm/dl), documented fever, penicillin or cephalosporin allergy, cases who have received antibiotics in last 48 hours and pregnancies with IUGR babies. A nonprobability convenience sampling technique was used. Simple randomization was done avoiding biasness and the cases were divided into 2 groups. Informed consent was taken from the cases. The necessary pre-operative investigations was done. Inj. Ceftriaxone 1gm. iv was given to the patients 30-60 minutes before the skin incision in Group A and after cord clumping in Group B.

No other antimicrobial agents were given unless a post-operative infection was diagnosed.

The duration of surgery was measured from skin incision up to complete skin closure. All cases were done under spinal anesthesia. Approximate blood loss during surgery was estimated by visual estimation by the obstetrician and nursing staff. Any intraoperative complication was noted.

The postpartum care for both groups was identical, all patients in both groups were observed daily to assess for any infectious complications (Fever, Endometritis, UTI, SSI) clinically. If the patient had clinical features, necessary investigations were done. The patients were discharged on the third postoperative day if there was no infection or complication, patients were followed up for 6 weeks, postpartum, so that infectious complications in the postpartum period following cesarean section were all included. The rates of postoperative infectious morbidity were compared between the two groups.

For detecting the outcome the following definitions were used –

a) Fever -Temperature of > 100.4^{o} F on two occasions 6 hours apart, excluding the first 24 hours of caesarean section. standard mercury thermometer were used.

b) Febrile morbidity- Persistent fever of at least 38^{o}C for at least 24 hours after surgery not associated with lower abdominal/pelvic tenderness and no signs of infection elsewhere.

c) Wound infection- Partial or total dehiscence or presence of purulent or serous wound discharge with induration, warmth and tenderness with or without fever, raised TC, CRP and /or positive pus culture.

d) Endometritis- Presence of fever with lower abdominal or uterine tenderness with tachycardia leukocytosis, sub-involution of uterus and foul smelling lochia, High Vaginal swab may/may not be done.

e) UTI- Presence of fever with a lower abdominal or flank pain, burning micturition and / or increased frequency of micturition with positive findings in urine analysis.

We also evaluated neonatal outcomes including need for admission to the neonatal intensive care unit, Apgar score less than 7 at 5 minute, neonatal sepsis and length of stay (day) in NICU. Neonatal sepsis was suspected if tachycardia and or tachypnea, as well as an increased white cell count with bands was present and confirmed by positive blood cultures. Length of hospital stay, admission status were determined by the neonatologists. Normality of the data was tested with Kolmogorov Smirnov and Chi-square tests when appropriate chi-square comparisons were performed for categorical variables. Analysis of variance testing was performed when multiple groups of categorical variables were encountered. Student' t' test were used for continuous variable analysis. Data were presented as mean + standard deviation for continuous variables and as frequency (percentage) for categorical variables. A' p' value of less than 0.05 was considered statistically significant.

Results :

There were a total of 1690 deliveries during the study period of which 410 (24.2%) had cesarean section, 181 cesarean deliveries were enrolled in this study, of the woman who were enrolled, three woman were excluded because they were incorrectly recruited with a duration of ruptured membranes exceeding 24 hours and two patients excluded as needed blood transfusion. The data of 176 women were actually analyzed in this study. Group A consisted 89 women and Group B consisted 87 women.

There were no significant differences in demographics between women in either group participating in the study (Table-I)

The indications for caesarean section were similar when two groups were compared (Table-II).

Two groups were comparable in terms of duration of labour, presence of premature rupture of membrane, per vaginal examination, duration of surgery and blood loss in surgery (Table-III).

Data are presented as n(%) except when stated otherwise. No significant difference in the type or severity of wound infection was observed between both groups (Table-IV), no case of endometritis in Group-A and one case in Group-B was observed. One case of UTI in Group-A and two cases in Group-B were observed. Febrile morbidity six cases in Group-A and five cases in Group-B were observed.

There were no significant differences observed between the two groups in 5-minute Apgar score, Neonatal sepsis, NICU admission and length of stay in NICU.

Table-I

Demographic Characteristics of the study groups

Characteristics	Group-A (n=89)	Group-B (n=87)	P- Value
Age (in year)	26.4	26.2	0.94
Gravidity (in number) IQR	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.75
Parity (in number) IQR	1.0(0.0-2.0)	1.0 (0.0-2.0)	0.6
Gestational age (in weeks)	38.9	38.5	0.46
BMI (kg/m^2)	24.7	24.6	0.84

IQR – Interquartile range

Table-II

Indication of Caesarean section

Indications	Group-A (n=89)	Group- B (n=87)	P- Value
Fetal Distress	23 (25.8%)	15(17.2%)	0.17
Cephalo-pelvic disproportion	21(23.6%)	24(27.6%)	0.49
Previous Caesarean section	8(9.0%)	8(9.2%)	0.96
Protracted labour	24(27.0%)	25(28.7%)	0.79
Placenta previa	1(1.1%)	1(1.1%)	0.6
Elective Caesarean section	6(6.7%)	5(5.7%)	0.77
Other	6(6.7%)	9(10.3%)	0.40

Table-III

Comparison of obstetric and surgical variable in the two groups

Variable	Group-A (n=89)	Group-B (n=87)	P- Value
Mean duration of labour in hour (IQR)	10.6 (0.0-11.9)	10.0 (1.0-12.0)	0.79
Mean duration of rupture of membrane in hour (IQR)	2.9(0.0-4.9)	3.3 (0.0-7.1)	0.09
Vaginal examination (in number)	3.3	3.4 +1.3	0.93
Operation time	45.3	48	0.07
Mean estimated blood loss(in ml)	878	875	0.18

Table-IV

Comparison of postoperative infectious morbidity

	Group-A (n=89)	Group-B (n=87)	P- Value
Wound infection (SSI)	6(6.7%)	9(10.3%)	0.40
Endometritis	-	1 (1.1%)	1.0
UTI	1(1.1%)	2 (2.2%)	0.5
Febrile morbidity	6(6.7%)	5(5.7%)	0.77

Table-V

Comparison of neonatal outcome

	Group-A (n=89)	Group-B (n=87)	P-value
Mean 5-minute Apgar score	9.08	9.06	0.79
Neonatal Sepsis(in number)	10(11.2%)	11 (12.6%)	0.77
NICU admission	15(16.7%)	15 (16.7%)	0.1
Length of stay (day) in NICU	7.0	7.2	0.67

Discussion:

The administration of antibiotics is not intended to sterilize tissues, but to act as an adjunct to decrease the intra-operative microbial load to a level that can be managed by the host's innate and adaptive immune responses [14].

However, in the case of cesarean section preoperative antibiotic dosing is associated with a substantial plasma level in the neonate [9]. So, it is common practice to delay antibiotic until the baby is delivered and the umbilical cord clamped. Costantine et al; [13] found significantly higher rates of endometritis and SSI in the group receiving antibiotics after cord clamping. But Zhang C et, al [12] have found no difference in the incidence of postpartum endometritis, wound infection and total puerperal morbidity. Also, no increase in the incidence of neonatal sepsis, septic workup, or intermediate NICU admission was observed.

In our study, we have found no significant difference in the incidence of postpartum wound infection (p-value=0.4), Endometritis (p-value= 1.0), UTI (p-value=0.5), Febrile morbidity (p-value=0.77) between the groups who received antibiotics prior to surgical incision and who received antibiotics after cord clumping. These results corresponds to the study conducted by Zhang C et, al.[12]

Regarding neonatal outcome no significant differences were observed between the two groups in 5-minute Apgar score (p-value=0.79), neonatal sepsis (p-value=0.77), NICU admission (p-value=0.1), and length of stay in NICU (p-value=0.67). These results also corresponds to the study conducted by Zhang C et, al.[12]

Strength of this study:

. The strength of this investigation was that it was a prospective randomized trial of patients with similar maternal demographics and similar intrapartum profiles of events that have been associated with the subsequent development of post-cesarean maternal and neonatal infectious morbidity. We have used a third-generation cephalosporin. In addition, the completion of this investigation in a single institution with the same team of surgeons probably increases the validity of our results.

Limitations of this study:

However, our study has several limitations, we could not detect vaginal colonization by group B streptococcus and anaerobic organism, so we could not cure these patients. It is possible that the results might have been different if an antibiotic other than ceftriaxone had been used. In study by Alekwe et al; in 2008[15] it was found that Single dose Ceftriaxone was as effective as a combination of ampiclox, gentamicin, and metronidazole in preventing post-elective cesarean section complications.

Conclusion:

Despite these limitations, it seems that time of antibiotic prophylaxis application does not change maternal infectious morbidity in cesarean deliveries. Preoperative prophylaxis application does not affect neonate morbidity rates as stated in literature. Well-designed randomized controlled studies including more cases are needed for examination of the effect of prophylaxis application time on maternal and neonatal results.

References:

1. Thorkild F. Nielsen, Klas-Henry Hökegård, Postoperative cesarean section morbidity: A prospective study, American Journal of Obstetrics and Gynecology, Volume 146, Issue 8, 1983, Pages 911-916, ISSN0002-9378, https://doi.org/10.1016/0002-9378(83)90963-8.
2. Leth RA, Møller JK, Thomsen RW, Uldbjerg N, Nørgaard M. Risk of selected postpartum infections after cesarean section compared with vaginal birth: a five-year cohort study of 32,468 women. Acta Obstet Gynecol Scand. 2009 Sep;88(9):976-83. doi: 10.1080/00016340903147405. PMID: 19642043.
3. Olivier Sibomana, Athanasie Bugenimana, Gabriel Ilerioluwa Oke, Ndayambaje Egide, Prevalence of post caesarean section surgical site infections in Rwanda: A systematic review and meta analysis, International Wound Journal, 10.1111/iwj.14929, 21, 5, (2024).
4. Smaill FM, Grivell RM. Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD007482. DOI: 10.1002/14651858. CD007482.pub3.
5. Martin C. Antimicrobial Prophylaxis in Surgery: General Concepts and Clinical Guidelines. Infection Control & Hospital Epidemiology. 1994;15(7):463-471. doi:10.1086/646952
6. Steinberg, James P. MD; Braun, Barbara I. PhD; Hellinger, Walter C. MD; Kusek, Linda RN, MPH; Bozikis, Michele R. MPH; Bush, Andrew J. PhD; Dellinger, E Patchen MD; Burke, John P. MD; Simmons, Bryan MD; Kritchevsky, Stephen B. PhD Trial to Reduce Antimicrobial Prophylaxis Errors (TRAPE) Study Group. Timing of Antimicrobial Prophylaxis and the Risk of Surgical Site Infections: Results From the Trial to Reduce Antimicrobial Prophylaxis Errors. Annals of Surgery 250(1):p 10-16, July2009. DOI: 10.1097/SLA.0b013e3181ad5fca
7. Festin M, Laopaiboon M, Pattanittum P, Ewens M, Henderson Smart D, Crowther C; Caesarean section in four South East Asian countries: Reason for rates associated care practices and health outcomes BMC pregnancy Childbirth 2009; 9: 17-43.

8. Tita A, Rouse D, Black well S, Saade G, Spong C, Andrews ; Emerging concepts in antibiotics prophylaxis for caesarean delivery. A systemic review. Obstet Gynecol2009; 113:675-82.

9. Fiore MT, Pearlman MD, Chapman RL, Bhatt Mehta V, Faix RG; Maternal and transplacental pharmacokinetics of Cefazolin. Obstet Gynecol 2001; 98: 1075-9.

10. Ayukekbong, J.A., Ntemgwa, M. & Atabe, A.N. The threat of antimicrobial resistance in developing countries: causes and control strategies. Antimicrob Resist Infect Control 6, 47 (2017). https://doi.org/10.1186/s13756-017-0208-x

11. Archar GL; Alteration of cutaneous Staphylococcal flora as a consequence of antimicrobial prophylaxis Rev Infect Dis 1991; 13 (suppl10): 8805-9 (Level - III).

12. Zhang C, Zhang L, Liu X, Zhang L, Zeng Z, Li L, et al. (2015) Timing of Antibiotic Prophylaxis in Elective Caesarean Delivery: A Multi-Center Randomized Controlled Trial and Meta-Analysis. PLoS ONE 10(7): e0129434. https://doi.org/10.1371/journal.pone.0129434

13. Costantine MM, Rahman M, Ghulmiyah L, Byers BD, Longo M, Wen T, Hankins GD, Saade GR. Timing of perioperative antibiotics for cesarean delivery: a metaanalysis. Am J Obstet Gynecol. 2008 Sep;199(3):301.e1-6. doi: 10.1016/j.ajog.2008.06.077. PMID: 18771991.

14. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Infection Control & Hospital Epidemiology. 1999;20(4):247-280. doi:10.1086/501620

15. Alekwe, L. O., Kuti, O., Orji, E. O., & Ogunniyi, S. O. (2008). Comparison of ceftriaxone versus triple drug regimen in the prevention of cesarean section infectious morbidities. The Journal of Maternal-Fetal & Neonatal Medicine, 21(9), 638–642. https://doi.org/10.1080/1476705080 2220490