

## The Efficacy of 3 Doses Versus 7 Days Course of Prophylactic Antibiotics following Caesarean Section - An Experience from A Tertiary Care Hospital

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### Abstract

**Introduction:** Surgical site infection (SSI) is one of the common problems following caesarean section. Antimicrobial prophylaxis is used to reduce the microbial burden of intraoperative contamination to a level that can not overwhelm host defenses. Amoxicillin-clavulanic acid is a broad spectrum antibiotic that is active against most of the organisms implicated in post-caesarean infections.

**Objectives:** The objective of the study was to evaluate the efficacy of 3 doses of amoxicillin-clavulanic acid (study group) versus a 7 days combination of amoxicillin-clavulanic acid and metronidazole (control group) as prophylactic antibiotics following caesarean section.

**Methods:** A randomized controlled trial conducted for a year from July 2019- June 2020 at Midnapore Medical College, India. Patients were randomly assigned in :

Group A: Those who received 3 doses of intravenous Amoxicillin-clavulanic acid 1.2 gm 12 hours apart with first dose given 30- 60 minutes before incision.

Group B: Those who received intravenous Amoxicillin-clavulanic acid 1.2 gm twice daily for 7 days along with 3 doses of intravenous metronidazole 8 hours apart.

**Results:** The distribution of mean age, mean weight, mean gestational age and parity were statistically not significant, hence placement of groups was homogenous in nature. E.Coli was the commonest microorganism responsible for SSI in both arms. Mean hospital bed occupancy and the mean cost of antibiotics was much less in Group A and is statistically significant ( $p < 0.05$ ).

**Conclusions:** The current study has demonstrated that short term prophylaxis is equally effective as with long term with the added benefit of reduced rate of acquiring nosocomial infections.

**Keyword:** SSI, ANTIBIOTIC PROPHYLAXIS, LSCS

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## Introduction:

Surgical site infection (SSI) is one of the most common problems following caesarean section and has an incidence between 3-15% [1, 2, 3]. Though the risk for developing SSI has significantly decreased in recent years due to improvements in hygiene conditions, antibiotics prophylaxis and sterile procedures [4, 5], with the overall increase in caesarean section rate in recent years, it is expected that the occurrence of SSI has increase in same fashion, hence its clinical significance. Post-caesarean wound infection is not only a major cause of prolonged hospital stay, but also an important cause of widespread aversion towards caesarean delivery in developing countries [6]. Caesarean section by itself is the single most important risk factor for postpartum maternal infection, as women undergoing caesarean delivery have 5-30 times greater risk of acquiring infection compared to vaginal delivery [7].

Apart from wound infection, other infectious morbidities that may complicates caesarean sections includes high fever, urinary tract infection, endometritis, bacteremia, pelvic vein thrombophlebitis, necrotizing fasciitis, pelvic abscess and many others including septic shock and all these may lead to increased maternal morbidity and mortality [7, 8]. Risk of infection may further be increased with prolonged labor, preterm and/or prolonged rupture of membranes, frequent vaginal examination, anemia, obesity and diabetes mellitus [7, 9].

Three main principles for preventing surgical site infection include preoperative skin antisepsis, sound surgical techniques and antimicrobial prophylaxis [8]. Antimicrobial prophylaxis used to reduce the microbial burden of intraoperative contamination to a level that can not overwhelm host defenses [10]. An adequate antibiotic level in the

tissue can augment natural immune defense mechanisms, kills microbes that inoculated in to the wound during operative procedures and decreasing postoperative morbidities both in low and high risk patients [7, 8]. However, injudicious uses of antibiotics not only causes untoward side effects and resistant strain of micro organisms, but also lead to higher cost of health care [11].

Amoxicillin-clavulanic acid is a broad spectrum antibiotic that is active against most of the organisms implicated in post-caesarean infections [11]. Prophylactic antibiotics for caesarean section can be expected to result in major reduction in postoperative infectious morbidity, but it is debatable which regime should be used that may capable of producing a desired result and cost effective. Moreover, increased duration of antimicrobial exposure may lead to colonization with resistant organisms so as is the use of combination antimicrobials [12]. Recent evidence suggests that administration of broad-spectrum antibiotic prophylaxis within 30-60 minutes prior to skin incision instead of after cord clamping is more advantageous with no untoward effects on the baby [13].

**Objectives:** The objective of the study was to evaluate the efficacy of 3 doses of amoxicillin-clavulanic acid (study group) versus a 7 days combination of amoxicillin-clavulanic acid and metronidazole (control group) as prophylactic antibiotics following caesarean section.

**Materials and Methods:** This was a randomized controlled trial conducted for a year from July 2019- June 2020 at Midnapore Medical College, a peripheral medical college of West Bengal in the department of G&O with ethical consent from higher authority. This medical college has a huge

catchment area with population came from nearby districts as referrals and also from adjacent states like Orissa, Bihar and Jharkhand round the year. The average yearly live birth delivery in this institution is approximately 14000-15000 and caesarean section around 4600-4900 per year.

**Study population:** Pregnant mothers carrying >37weeks to <42 weeks attended OPD, emergency or admitted in labor ward and decided to undergo emergency/ elective caesarean section were included in the study.

Patients were randomly assigned in to one of the two groups by software generated random number that was serially allocated in opaque sealed envelope:

**Group A:** Those who received 3 doses of intravenous Amoxicillin-clavulanic acid 1.2 gm 12 hours apart with first dose given 30-60 minutes before skin incision.

**Group B:** Those who received intravenous Amoxicillin-clavulanic acid 1.2 gm twice daily for 7 days along with 3 doses of intravenous metronidazole 8 hours apart.

Pregnant women who were allergic to the drugs, those carried with established infections before surgery or already continued with antibiotics due to some other illness, with more than one prior caesarean section, with prolonged rupture of membranes, had obstructed labor, who had more than 6 vaginal examination and known diabetics were excluded from the study.

Group A (study group) comprised of 75 patients who received 3 doses of intravenous Amoxicillin-clavulanic acid 1.2 gm each 12 hours apart with first dose given 30-60 minutes before the commencement of skin incision. No additional antibiotics were given. Those who developed infectious morbidity were evaluated and treated accordingly.

Group B (control group) also comprised of 75 patients received intravenous Amoxicillin-clavulanic acid 1.2 gm postoperatively twice daily for 7 days with additional intravenous metronidazole 8 hourly for first 24 hours.

Patients of both groups were managed postoperatively in same fashion. Urethral catheters were removed in both groups after 24 hours. Wound was inspected on 5th postoperative day to detect any sign of infection with few exceptions like persistent high fever, marked tenderness at the operated site or soakage of the dressing over the wound. Signs of infection include serous or purulent exudates from the wound with or without separation of underlying tissues. Endometritis was diagnosed in patients with high temperature, tachycardia, foul smelling lochial discharge with uterine tenderness; diagnosis to be confirmed with positive high vaginal swab culture. Sterile cotton-tipped swab with transport medium were used for wound swab and abnormal lochial sampling. Those patients who were found well were discharged on day five or day seven depending upon the type of skin incision used. Those patients found to have wound infection were kept admitted for further evaluation and treatment.

**Statistical analysis:** Data obtained was analyzed using Statistical Package for Social Sciences (SPSS) version 23. Quantitative variables were described using means and standard deviation whereas qualitative variables by percentages. Categorical variables (qualitative) were analyzed using Chi-square test while continuous variables (quantitative) were analyzed using independent sample t-test. A p-value was considered significant when it is <0.05.

**Results and Analysis:** A total of 150 patients, divided in to two groups, Group A and Group B, were allotted in this trial and randomly selected to any of the group. The mean age of randomized women in group A

and group B was  $26.6 \pm 0.254$  and  $27.24 \pm 0.241$  years respectively which is statistically not significant. Similarly mean weight in group A was  $61.68 \pm 1.45$  kg and group B, it was  $63.09 \pm 1.76$  kg, the difference

also statistically insignificant. The distribution of mean gestational age and parity also statistically not significant, hence placement of groups was homogenous in nature.

**Table 1: Demographic characteristics among the groups**

Variables	Group A	Group B	p-value
Mean age (years) $\pm$ SD	$26.653 \pm 0.254$	$27.248 \pm 0.241$	0.1456
Mean weight (kg) $\pm$ SD	$61.68 \pm 1.45$	$63.09 \pm 1.76$	0.049
Mean gestational age (weeks) $\pm$ SD	$38.145 \pm 2.32$	$38.432 \pm 1.98$	0.243
Mean parity $\pm$ SD	$1.813 \pm 0.12$	$1.876 \pm 0.34$	0.165
Booked patients	19	27	0.1566
Unbooked patients	56	48	0.1566

Majority of the caesarean sections were done in primigravida group and commonest indication was severe preeclampsia. Second most common indication was post-caesarean pregnancy.

**Table 2: Indication for caesarean section between the groups**

Indication	Group A	Group B	p-value
Severe preeclampsia	31	36	0.611
Post CS	15	19	0.53557
APH	05	02	0.2455
Malpresentation	06	05	0.75411
Meconium stained liquor	08	07	0.785
Failed induction	10	06	0.09

Majority of the surgeries in two arms were emergency caesarean deliveries. Major portion of the patients had spinal or epidural anesthesia and suprapubic low transverse incision had given to most of the patients irrespective of groups. Mean operating time in group A was  $52.29 \pm 2.21$  minutes whereas in group B, it was  $55.06 \pm 1.98$  minutes. The amount of mean blood loss in group A was  $457.75 \pm 11.89$  ml and  $468.27 \pm 15.67$  ml in group B.

**Table 3: Operative variables among the two groups**

Variables	Type	Group A	Group B	p-value
Type of CS	Emergency	47	52	0.388
	Elective	28	23	0.388
Type of anesthesia	Spinal/Epidural	65	69	0.29
	General	10	06	0.29
Type of skin incision	Low transverse	71	70	0.73
	Infra-umbilical midline	04	05	0.73
Mean operating time (min) $\pm$ SD		$52.29 \pm 2.21$	$55.06 \pm 1.98$	0.039
Mean blood loss(ml) $\pm$ SD		$457.75 \pm 11.89$	$468.27 \pm 15.67$	0.1345

Overall, 16 women had surgical site wound infection out of 150 patients (10.66%) of which 7 cases were in group A and 9 cases were in group B. E.Coli was the commonest microorganism responsible for SSI in both arms.

**Table 4: Bacterial patterns responsible for post caesarean wound infection**

Bacterial type	Group A	Group B	p-value
Staph aureus	02	01	0.559
E. coli	03	04	0.6073
Klebsiella group	01	01	1
Pseudomonas	01	02	0.4735
Total	07	09	0.4772

Apart from wound infection, urinary tract infection was the commoner form of infectious morbidity. Post operative febrile condition was defined as an axillary temperature of 38 degree C on two occasions at least 6 hours apart, excluding first 24 hours. Wound infection was considered with presence of serous or purulent wound discharge with or without disruption of skin layer. Endometritis was diagnosed when there was uterine tenderness with foul smelling lochial discharge in addition to fever.

**Table 5: Infectious Morbidities associated with each group**

Type of morbidity	Group A	Group B	p-value
Fever	09	12	0.4802
Endometritis	04	06	0.5126
Urinary tract infection	10	07	0.4396
Wound infection	07	09	0.2799

Mean hospital bed occupancy in Group A was 5.153±0.24 days and 7.84±1.28 days in Group B which is statistically significant. It is interesting to note that there was remarkable difference of mean cost of antibiotics between group A and in group B which is statistically highly significant.

**Table 6: Other Maternal Variables among the Groups**

Type of variable	Group A	Group B	p-value
Mean hospital stay (days) ±SD	5.153±0.24	7.84±1.28	0.003
Mean cost of antibiotics per patient (Rs) ±SD	610.00±22.00	1967.00±31.00	0.0024
Maternal Minor side effects	07	13	0.1495

There was no major difference in mean birth weight of newborn among the groups, nor the mean Apgar scores. SNCU admission in Group A was 11 and that of Group B was 9, but again it was statistically insignificant.

**Table 7: Neonatal Outcome**

	Group A	Group B	P value
Mean birth weight (kg) ±SD	2.6853±0.25	2.7314±0.34	0.453
Mean Apgar score±SD	8.5±1.1	8.7±0.9	0.71
SNCU admission	11	09	0.63095

## Discussion:

The current study clearly showed that there was no significant difference in outcome in patients having 3 doses of intravenous Amoxicillin-clavulanic acid 1.2 gm 12 hours apart (**Group A**) with those who received intravenous Amoxicillin-clavulanic acid 1.2 gm twice daily for 7 days along with 3 doses of intravenous metronidazole 8 hours apart (**Group B**). Similar type of randomized controlled trials by other researchers concluded the similar findings [14,15,16]. World health organization [17] and Royal College of Obstetrician and Gynecologist [18] also recommended for short term antibiotic prophylaxis for caesarean section.

The overall surgical site wound infection rate in our study was 10.66% which was much lower than the studies of other researchers like Onyegbule OA et al [12.5%] (19) and Morhason-Bello IO et al [16.2%] (20). The lower rate of infection may be due to exclusion of patients with prolonged rupture of membranes with chorioamnionitis, had obstructed labor, who had more than 6 vaginal examinations and known diabetics from the study group.

Multiple and repeated vaginal examination is a well established risk factor for occurrence of endometritis [21,22]. The rate of endometritis lower in our study among both the groups. Restricted vaginal examinations in our study subjects may be a key factor for lower infection rate.

In our study, the commonest organism isolated from wound infection was E. coli and Staph aureus was the second common. This was not matched with the study of Agboeze J et al where the commonest organism found in post caesarean wound swabs in their subjects were S. aureus [23]. The perineal habits of patients may have played a role in increased prevalence of E.Coli. Good post operative perineal hygiene

has been shown to decrease the incidence of postoperative surgical site infection [24]. It should be noted that patients infected with P. aeruginosa and Klebsiella species had stayed for longer period in hospital compared to patients infected with E. Coli and Staph aureus.

Mean duration of hospital stay in Group A was  $5.153 \pm 0.24$  days and  $7.84 \pm 1.28$  days in Group B which is statistically significant ( $p < 0.05$ ). This is one of the main advantages of short term antibiotic prophylaxis as patients have to be admitted for shorter number of days and comparable with the study done by Ayangade O et al [25]. Other advantages of this regime are, oral medications can be started much earlier than the long term prophylaxis group and less chance of acquiring nosocomial infections [26].

The mean cost of antibiotics was much less in short arm group i.e. Group A (Rs  $610.00 \pm 22.00$  vs. Rs  $1967.00 \pm 31.00$ ) and is statistically significant ( $p < 0.05$ ). The reason is simple, that is use of costly antibiotics for longer days in Group B. Thus, the policy of short term antibiotics is an effort to curtail the medical costs was reasonable and comparable with the study done by Ayangade O [25].

Table -7 showed the different variables of neonatal outcome including birth weight, Apgar scoring and SNCU admission between the two groups. The statistical difference was insignificant; hence no clear advantage has elicited by long term prophylaxis over the short term.

**Limitation:** To know the utility of this study, it would be the need for more similar studies with larger samples. Another difficulty in determining preclinical endometritis was a limitation to this study as only those presented with symptoms were included for endometritis and those were not, were excluded, so there is chance of sampling bias.

## Conclusions:

The current study has demonstrated that short time antibiotic prophylaxis is equally effective as long-term prophylaxis in preventing post caesarean wound infection and endometritis. Short term prophylaxis also has the added benefit of being cost effective, shorter duration of hospital stay and reduction rate of acquiring nosocomial infections.

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