Role Of Pre-cesarean Section Amoxicillin with Ceftriaxone in Ameliorating Post-cesarean Infection: A Comparative Study

Anum Asad Ullah,[1] Saira Iqbal,[2] Fatima Jabeen,[3] Faiza Ijaz,[4] Amara Khalid,[5] Maria Sharif[6]

Abstract

Objective: The objective of study was to assess whether preoperative administration of two broad-spectrum antibiotics (Amoxicillin vs Ceftriaxone) used a preventive measure against the maternal wound infection after CS are equally efficient against wound infection. Caesarean sections (CS) and surgical vaginal births are established risk factors for maternal infection. Surgical site infections (SSIs) happens to be a common entity and can be avoided with the use of appropriate antibiotic prophylaxis which can be given in pre/intra/post-operative period. Despite available guidelines on preoperative antibiotics prophylaxis, there are obstetricians' preferences in antibiotic selection in clinical practice. There is insufficient evidence to support the use of selective prophylaxis as current WHO recommendations do not endorse such antibiotic prophylaxis for women having uncomplicated surgical vaginal births.

Method: The study lasted for six months and was conducted in the Department of Obstetrics & Gynecology, Lady Atchison Hospital, Lahore. This comparative study was conducted with 482 subjects (aged ⩾16 years) from single centered tertiary care hospital, in Lahore. Women were randomly allocated into two groups; each group contain 241 participants; Group 1: was given amoxicillin before and after CS; Group 2: was given ceftriaxone before and after CS. The primary outcome of the treatment was the presence/absence of maternal infection.

Results: In the amoxicillin-received group (n=241), only 4 (1.7%) female got wound infections compared to 6 (2.5%) women of the ceftriaxone-treated group (n=241) (OR=0.751, 95% CI=0.209-2.695, p-value= 0.659).

Conclusion: In low-resource settings, a simple dosage of prophylactic amoxicillin or ceftriaxone have the same efficacy and effectiveness for preventing post-caesarean wound infections therefore both can be considered an effective prophylactic to reduce the risk of post-caesarean wound infection in the local population.

Keywords: Caesarean section, ceftriaxone, wound infection, surgical site infection, amoxicillin

How to cite: *Ullah AA, Iqbal S, Jabeen F, Ijaz F, Khalid A, Sharif M. Role Of Pre-cesarean Section Amoxicillin With Ceftriaxone In Ameliorating Post-cesarean Infection: A Comparative Study. Esculapio - JSIMS 2023;19(01):105-109*

DOI: https://doi.org/10.51273/esc23.2519122

Introduction

The frequency of caesarean sections has been increasing in the last decades, both in the USA and the Asia-Pacific region.[1,2] A substantial cause of maternal morbidity and probable fatality is infections and their related complications following obstetric surgery. Caesarean delivery is the only primary risk factor for post-partum maternal infection. Women having caesarean deliveries have a five to twentyfold increased risk of infection and infectious morbidity as compared to vaginal births.[3] Generally, 70% of the total women cases with maternal mortality have severe sepsis, infection, and low survival rate with long-term health issues.[4] About 11% of maternal mortality worldwide is because of severe sepsis and infections.[5] However, 20,000 mortality cases because of pregnancy-related infections have been reported annually.[6] The pregnancy-related infection

1. *Lady Aitchison Hospital, Lahore. Pakistan*
2. *BHU Kotli Khokharan. Pakistan*
3. *BHU Loharwala. Pakistan*
4. *Social Security Hospital Sheikhupura. Pakistan*
5. *BHU Khairpur Daha. Pakistan*
6. *DHQ South City Okara. Pakistan*

Correspondence:
Anum Asad Ullah (FCPS), *Women Medical Officer, Lady Aitchison Hospital, Lahore. Pakistan. Email: anumkhan45@hotmail.com*

Submission Date:	17-02-2023
1st Revision Date:	25-02-2023
Acceptance Date:	15-03-2023

mortality varies globally and is reported higher in most low-income countries than in developed countries. Only USA and other nations have maternal mortality of 13% - 05% respectively.[7] A WHO global study and awareness campaign is focusing on undertreated and under-recognized maternal infection-based mortality.[8]

To lower the rate of post-caesarean surgical site infections (SSIs), surgical patients, particularly caesarean patients, have been recommended for use of proper surgical antibiotic prophylaxis as part of SSI prevention bundles.[9] Due to concerns that earlier administration of antibiotic prophylaxis for caesarean delivery would expose fetuses through the placenta, this practice has typically been performed after clamping the umbilical cord.[10] Maternal sepsis-causing risk factors may be identified from Caesarean section and operative vaginal. According to estimates, up to 16% of women who give birth via surgical vaginal delivery and 20–25% of women who give birth via caesarean section both get an infection without prophylaxis. Meta-analysis has revealed that the chances of endometritis, wound and maternal infections may be reduced by about 60-70% subject to the administration of prophylaxis.

The prophylaxis may be administrated an hour before the incision to ensure the availability of optimized concentration in the blood and tissue.[11,12] Intraoperative redosing is suggested when the antibiotic has more than two half-lives since the initial dosage of prophylaxis was administered because the probability of SSIs increased subjected to redosing during a lengthy procedure. Additionally, substantial perioperative bleeding required redosing during surgery.[12,13] Obese patients may require increased concentration for the availability of the optimum concentration of drug in tissue.[14] Despite the existence of defined standards for preoperative antibiotic prophylaxis, there are still variations in clinical procedures depending on the choice of obstetricians. Taking into account the importance of prophylaxis, the present study was planned to examine and compare the efficacy of two important antibiotics (amoxicillin, ceftriaxone) administration before caesarian section in avoiding post-operative wound infection and related complications.

Material and Method

The study lasted for six months and was conducted in the Department of Obstetrics & Gynecology, Lady Atchison Hospital, Lahore. The study was dully approved by from Ethical review board of the institute in accordance with the declaration of Helsinki. Before the enrolment, each participant was informed about the study, and consent was taken from each participant. A sample size of 482 was calculated with 80% power of the test, 90% confidence interval (CI), and taking an expected percentage of wound infection as 1% with amoxicillin and 4.8% with ceftriaxone.[15,16] Patients with ages ranging 18-40 years with parity <5 undergoing elective caesarean section (due to previous C-section, short stature, cephalopelvic disproportion (on ultrasound) were included while patients presented with gestational/chronic diabetes (BSR>186mg/dl), hypertension (BP ≥ 140/90mmHg), Anemic (Hb ≤ 10mg/dl), INR >2, PT 20sec and APTT >15sec were excluded from the study. All the participants were physically examined for Body mass index (BMI) at the time of admision. The participants were divided into two groups labeled as amoxicillin-treated and ceftriaxone treated. Each participant in each represented group was administrated with 1 gm intravenously respected dose i.e. amoxicillin or ceftriaxone after cord clamping and repeated for three days after 1st dosage followed by oral administration of tablets (amoxicillin 250mg/ cefuroxime 250mg) 6 hourly for four days. After the performance of caesarean sections, all the subjects were kept under observation for 10 days until the removal of the suture followed by an assessment of wound inspection for the presence of infection. All statistical analyzes were performed using Statistical Package for the Social Sciences (SPSS) version. 21 (SPSS Inc. Chicago, IL). Mean, the standard deviation was used for demographic parameters while the Chi-square test was used to estimate the risk of wound infection in both groups with parameters maternal age, gestational age, parity, and BMI followed by posthoc sub-group analysis. Odds ratio (OR), 95% Confidence Interval (CI) was used with a level of significance less than 0.05.

Results

A total of 482 females with a mean age of 29.56±6.62 years were recruited. The demographics and clinical information were collected and are presented in (Table-1).

The mean age of amoxicillin treated group was 29.44± 6.53 while the mean age for ceftriaxone was 29.61 ± 6.75 years (Figure 1A). The gestational age at the time of CS was 37 weeks for n=125 and 38 weeks for n=116 cases for amoxicillin treated group while n=112 and n=129 cases for ceftriaxone treated group respectively (Fig-1B). The majority of the patients had normal Basal metabolic index (BMI) and half of the patients in both groups were primigravida. Both group cases n=237

(98.3%) and n=235 (97.5%) for amoxicillin and ceftriaxone respectively showed resistance toward post-operative wound infection.

Table 1: *Demographics and Clinical information of studied subjects (n=482)*

Demographics	Amoxicillin Treated group (n=241)	Ceftriaxone Treated group (n=241)
Maternal Age (years)	29.44±6.53	29.61 ±6.75
18-30	127 (52.7%)	129 (53.5%)
31-40	114 (47.3%)	112 (46.5%)
Gestational age (weeks) At randomization		
36-37	125 (51.9%)	112 (46.5%)
37-38	116 (48.1%)	129 (53.5%)
Body Mass Index (BMI) kg/m2		
18-24 (Normal)	180 (74.7%)	184 (76.3%)
25-29 (Overweight)	58 (24.1%)	53 (22%)
>30 (Obese)	03 (1.2%)	04 (1.7%)
Parity		
Multigravida	119 (49.4%)	110 (45.6%)
Primigravida	122 (50.6%)	131 (54.4%)
Post-Operative Wound Infection		
Present	4 (1.7%)	6 (2.5%)
Absent	237 (98.3%)	235 (97.5%)

Table 2 represented the risk factors associated with postoperative wound infections. All the variables including age (OR=0.751, 95%CI=0.209-2.695, p=0.659), parity (OR=2.144, 95%CI=0.548-8.390, p=0.262), gestational age (OR=1.462, 95%CI=0.407-5.249, p= 0.558) were found insignificant with the risk of wound infection (Table. 2) while BMI found significantly associated (p=0.0001) with the wound infection. Sub-group posthoc analysis has shown that patients with Higher BMI values have a high risk for surgical site infection after caesarian section (p=0.0001).

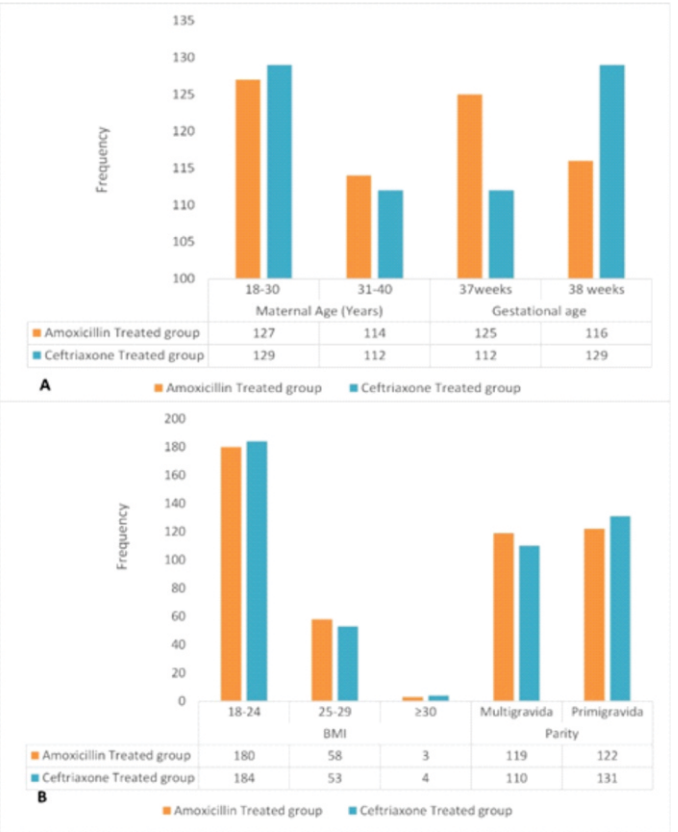

Fig-1. *Bar charts represented the frequencies of age, gestational age (A) and BMI and Parity (B)*

Table 2: *Correlation of outcomes with treatment (Amoxicillin vs Ceftriaxone), [OR: odds ratio; CI: confidence interval; p-value is considered as statistically significant when ≤0.05 (in bold)].*

Vari-able	Category	Wound infection present (Amoxi-cillin)	Wound infection absent (Amoxi-cillin)	OR (95% CI)	p-value	Wound infection present (Ceftria-xone)	Wound infection absent (Ceftriaxone)	OR (95% CI)	p-value	(OR (95%CI) Overall	p-value Overall
Age (years)	18-30	3 (2.4%)	124 (97.6%)	0.366 (0.38-3.567)	0.368	3 (2.3%)	126 (97.7%)	1.156 (0.229-5.845)	0.861	0.751 (0.209-2.695)	0.659
	31-40	1 (0.9%)	113 (99.1%)			3 (2.7%)	109 (97.3%)				
Parity	Multigravida	1 (0.8%)	118 (99.2%)	2.975 (0.305-29.01)	0.325	2 (1.8%)	108 (98.2%)	1.701 (0.306-9.466)	0.540	2.144 (0.548-8.390)	0.262
	Primigravida	3 (2.5%)	119 (97.5%)			4 (3.1%)	127 (96.9%)				
BMI (kg/m^2)	18-24	0	180 (100%)	N/A	**0.0001**	0	184 (100%)	N/A	**0.0001**	N/A	**0.0001**
	25-29	1 (1.7%)	57 (98.3%)			2 (3.8%)	51 (96.2%)				
	>30	3 (100%)	0			4 (100%)	0				
Gesta-tional Age (Weeks)	36-37	1 (0.8%)	124 (99.2%)	3.292 (0.338-32.10)	0.278	3 (2.7%)	109 (97.3%)	0.865 (0.171-4.374)	0.861	1.462 (0.407-5.249)	0.558
	37-38	3 (2.6%)	113 (97.4%)			3 (2.3%)	126 (97.7%)				

Discussion

Caesarean delivery (CD) is linked to a greater postoperative infection rate compared to vaginal birth and other surgical procedures. As CD prevalence rises globally, such post-CD infections are anticipated to constitute a serious health and financial burden. Results from past research have clear evidence that CD antibiotic prophylaxis works to reduce maternal infection morbidity along with cost-effective treatment. These advantages extend to both scheduled and unscheduled (emergency or laboring) CD. A single selective antibiotic may have equal effectiveness compared to multiple doses of a combination of antibiotics.[9] The best medication for surgical prophylaxis should be long-acting, affordable, and have few side effects.[9,17] The most used antimicrobial for prophylaxis in obstetricians is usually cephalosporin. Ceftriaxone and Amoxicillin and other similar class of antibiotics has already been proven to be effective antibiotics for the prevention of postoperative infection morbidities after caesarean section by numerous earlier research.[18,19]

In this study, we compared the effectiveness of preoperative administration of two important preventive antibiotics at cord clamping, with the primary outcome as the presence of wound infection after CS birth. We had to use an intravenous dose of 1gm for four days followed by oral administration of 250mg 6-hourly for both antibiotics in their respective treated group cases. Our study provided data on the frequency of surgical site infections in a hospital where prophylactic antibiotic administration before skin incision and consistent weekly operating room cleanliness was observed. The overall rate of 4 (1.7%) and 6 (2.5%) for amoxicillin and ceftriaxone respectively, is low when compared to the prevalence of SSI in developing nations, but this is also plausible because certain studies conducted in hospitals with good medical equipment have revealed even lower incidence. Both prophylaxes have shown insignificant differences while observing protective effects against wound infection. Interestingly, the morbidity rate in our trial was found lower as compared to the study of Igwemadu et al. and Mohn et al. where they reported 7.4% and 5.8% morbidity rates respectively.[20,21] Our findings are also strengthened by the previously reported studies in Asian ethnicities by Mudholkar et al.[22] and Ansari et al.[23] where they reported 0.3% and 2% cases respectively, of surgical wound infection.

Due to the poor socioeconomic status of the participants, the average low number of prenatal visits, and the likelihood of lengthy labor before surgery, our study population could be considered to have a high risk for infection given the recognized risk factors for postcesarean infection. Additionally, because most women only visit the hospital during labor, a significant portion of caesarean sections performed in low-resource settings can be categorized as emergency operations with a higher risk of infection than elective procedures. Taking into account all the liable factors for infections and other complications, both prophylaxes have shown significant protective effects in the local population hence the treatment can be used for the general population in the future based on further studies with a large sample size.

The only limitations of this study are the small sample size and single center. Additionally, following the Helsinki declaration (1975), amended in 2000, the current study received complete approval from the institute's ethical review board.

Conclusion:

In conclusion, the present study revealed the significance of the use of prophylactic (amoxicillin and ceftriaxone) as a preventive measure for post-operative caesarean wound infection in women. BMI was significantly associated with the risk of wound infection. However, because of the lower number of SSI that we anticipated and the tendency to have more cases in the group, we recommend the conduct of a rigorous multicenter study or a study with a large sample size confirming the absence of any difference in both groups. Further studies with other prophylactics may provide a pathway to the policymakers for constructing a strong policy regarding public health.

Conflict of Interest: *None*

Funding Source: *None*

References

1. Osterman MJ, Martin JA. Trends in low-risk cesarean delivery in the United States, 1990-2013. 2014.
2. Verma V, Vishwakarma RK, Nath DC, Khan HT, Prakash R, Abid O. Prevalence and determinants of caesarean section in South and South-East Asian women. PloS one. 2020;15(3):e0229906.
3. Kruit H, Mertsalmi S, Rahkonen L. Planned vaginal and planned cesarean delivery outcomes in pregnancies complicated with pregestational type 1 diabetes–A three-year academic tertiary hospital cohort study. BMC Pregnancy and Childbirth. 2022;22(1):173.

4. Acosta CD, Kurinczuk JJ, Lucas DN, Tuffnell DJ, Sellers S, Knight M, et al. Severe maternal sepsis in the UK, 2011–2012: a national case-control study. PLoS medicine. 2014;11(7):e1001672.
5. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014;2(6): e323-e33.
6. Naghavi M, Abajobir AA, Abbafati C, Abbas KM, Abd-Allah F, Abera SF, et al. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. The lancet. 2017; 390(10100): 1151-210.
7. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-related mortality in the United States, 2011–2013. Obstet Gynecol. 2017;130(2):366.
8. Bonet M, Souza JP, Abalos E, Fawole B, Knight M, Kouanda S, et al. The global maternal sepsis study and awareness campaign (GLOSS): study protocol. Reprod. Health. 2018;15(1):1-17.
9. Smaill FM, Grivell RM. Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section. Cochrane Database Syst. Rev. 2014(10).
10. Tita AT, Rouse DJ, Blackwell S, Saade GR, Spong CY, Andrews WW. Evolving concepts in antibiotic prophylaxis for cesarean delivery: A systematic review. Obstet Gynecol. 2009;113(3):675.
11. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. JAMA surgery. 2017;152(8): 784-91.
12. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect. 2013;14(1):73-156.
13. Kasatpibal N, Whitney JD, Dellinger EP, Nair BG, Pike KC. Failure to redose antibiotic prophylaxis in long surgery increases risk of surgical site infection. Surg Infect. 2017;18(4):474-84.
14. Sirard S, Abou Chakra CN, Langlois M-F, Perron J, Carignan A, Valiquette L. Is Antimicrobial Dosing Adjustment Associated with Better Outcomes in Patients with Severe Obesity and Bloodstream Infections? An Exploratory Study. Antibiotics. 2020;9(10):707.
15. ARSHAD I, NAWAZ R, NAZ T. Comparison of Efficacy of Ceftriaxone Alone or Combination with Metronidazole in Prevention of Wound Infection in Elective Cesarean Section. P J M H S. 2020.30(6.84):29.10-6. 95.
16. Ibrahim WH, Makhlouf AM, Khamis MA, Youness EM. Effect of prophylactic antibiotics (Cephalosporin versus Amoxicillin) on preventing post caesarean section infection. J. Am. sci. 2011;7(5):178-87.
17. ACOG Practice Bulletin No. 199: Use of Prophylactic Antibiotics in Labor and Delivery. Obstetrics & Gynecology. 2018;132(3):e103-e19.
18. Das S, Kundu R, Chattopadhyay BP. Comparison of single dose versus multiple doses of antibiotic prophylaxis for prevention of surgical site infection. Int J Surg. 2022; 9(1):129-32.
19. Jawad MJ, Hassan SM, Obaid AK, Hadi NR. Role of pre-cesarean section cefotaxime in ameliorated post-cesarean complication. Wiad Lek. 2022;75(4):818-23.
20. Igwemadu GT, Eleje GU, Eno EE, Akunaeziri UA, Afolabi FA, Alao AI, et al. Single-dose versus multiple-dose antibiotics prophylaxis for preventing caesarean section postpartum infections: A randomized controlled trial. Women's Health. 2022;18:1-7.
21. Mohan J, Thangaroja T, Menon M. Single dose antibiotic prophylaxis in elective obstetric and gynaecological surgeries-a descriptive study. IJRCOG. 2017; 6(9): 3897-903.
22. Mudholkar A, Taralekar V, Panchanadikar T, Wagh G. Study of prophylactic single dose of antibiotic in obstetric & gynaecological procedures in low risk patients. Indian J. Appl. Res. 2013;3:284.
23. Ansari N, Das C, Ansari MA. Evaluation of prophylactic antibiotic in caesarean section. Nepal Med Coll J. 2014; 12(2):40-1.

Authors Contribution

AAU: Conceptualization of Project
SI: Data Collection
FJ: Literature Search
FI: Statistical Analysis
AK: Drafting, Revision
AAU, MS: Writing of Manuscript