Temporal Comparison of Antibiotics Administration for Caesarean Section: A Prospective Randomized Study in Baghdad

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Abstract

Objectives: To compare the efficacy of antibiotic administration prior to skin incision and after clamping of umbilical cord as attempt for preventing the rates of maternal post-caesarean infectious morbidities and adverse neonatal outcomes.

Methods: In this prospective randomized study design, 100 pregnant women prepared to undergo CS were randomized evenly into two groups based on time they received prophylactic antibiotics either half to one hour prior to skin incision (group-1) or immediately after cord clamping (group-2). The post-caesarean maternal infectious morbidities are the primary outcomes, whereas neonatal infectious morbidities are secondary outcomes.

Results: Postpartum maternal infectious outcomes (fever, SSI, wound dehiscence, endometritis, UTI) were significantly lower in pre-incision group as compared to post-cord clamping group as well as the mean of maternal hospital stay respectively ($P< 0.05$). In spite the secondary neonatal outcomes found to be comparable among study's groups, but such differences did not reach the statistical significant.

Conclusion: Apart from neonatal outcomes, preoperative administrations of antibiotic significantly reduce the maternal post-caesarean infectious morbidities in comparison to its intraoperative administration.

Keyword: *Caesarean section, prospective, prophylactic antibiotic, endometritis, surgical site infection, neonatal sepsis.*

Introduction

Recently, a remarkable upsurge in the rate of caesarean-section has been reported worldwide. In Iraq, the overall caesarean-section rate reached 24.4% in 2012[1] which much higher than that of 5-15% recommended by World Health Organization (WHO)[2].

The increased risk of postoperative infections after caesarean-section delivery has been well identified, causing 5 to 20 folds increase in infection rates in comparison with normal vaginal delivery[3, 4].

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Post-caesarean infection may increase maternal mortality and morbidity, but fortunately it has been declined in last decades due to improvements in hygienic conditions, using prophylactic antibiotic and other antisepsis measures[5].

Prophylactic antibiotics are constantly associated with caesarean delivery and often used universally. The beneficial effect of antibiotics usage in reducing the post-caesarean infectious morbidity and mortality either planned or emergent is well established[6] covering 75% of post-caesarean infectious morbidity reduction incidence[7].

Among the most common infectious complications associated with caesarean delivery are; surgical site

infection (SSI), endometritis, fever, and urinary tract infections. SSI and endometritis are hitherto the most significant causes of post-caesarean infectious morbidity with the incidence of endometritis range between 20%-85% and 25% for wound infection particularly without antibiotic prophylaxis[8]. According to WHO, prophylactic antibiotics found to make a substantial reduction in the incidence of post-caesarean endometritis by two thirds to three-quarters of cases and up to three quarters for the incidence of wound infections, similarly, postpartum febrile morbidity and UTIs incidences are decreased[9].

The most common prophylactic antibiotics used is ceftriaxone which is third-generation cephalosporin [4]. As broad-spectrum antibiotics, its usage was associated with statistically significant reduction in infection rates of both endometritis and SSI as compared to narrow-range antibiotic prophylaxis. Furthermore, the length of hospital stay was also significantly shorter by using broad-spectrum antibiotics[5].

The current point of debate among literature is the timing of prophylactic antibiotics administration, taken in consideration that single-dose prophylaxis has been accepted, which may be administered 30-60 minutes prior skin incision owning to get optimal concentration at the surgical site thus reducing SSI, or administrated intra-operatively after clamping of umbilical cord for apprehension of fetal exposure to antibiotic through placenta that could potentially mask neonatal infection and their blood culture findings and thereby interferes with proper treatment in addition to emergence of resistant strains[3, 6, 10].

Therefore, the aim of this study is to compare the efficacy of ceftriaxone administration prior to skin incision and after clamping of cord as attempt for preventing the rate of maternal post-caesarean section infectious morbidities and adverse neonatal outcomes.

Methods

The current prospective randomized study was conducted in the Gynecology and Obstetrics Department of Al-Hayat private hospital for Dominican-Sisters of Saint Catherine in Baghdad city, Iraq over a two months period from March through May 2019. All pregnant women ≥37 weeks of gestational age who admitted for labour and fulfilled eligibility criteria added to giving written consent and had a decision for caesarean delivery (planned or emergent) were included in the study, the 37 weeks of gestation was chosen in order to avoid bias that pre-maturity is potential risk for adverse perinatal outcomes.

Pregnant women who were allergic Cephalosporin, those who had ruptured membranes >12 hours either with or without antibiotic-prophylaxis, those who received antibiotics within a week prior to caesarean delivery for any reasons, those pregnant with chronic diseases such as heart disease, renal disease or diabetes-mellitus, and those who were febrile from unknown origin were excluded from the study.

Incisively 120 pregnant women were enrolled in the study who were 37 gestational weeks admitted to hospital and provided written consents for participation. Afterward, detailed history regarding socio-demographic characteristic including age and parity, detailed current and past obstetrical, medical, surgical and menstrual histories were taken followed by rigorous general and obstetric examinations were done. Then 11 pregnant women were excluded who not-fulfilled inclusion criteria and 9 women were refused to participate.

Ultimately, a total 100 pregnant women who constitute the study's sample size were allocated randomly into two groups: Group-1 consist of 50 women who received 1-gram of ceftriaxone injection intravenously 30-60 minutes prior to skin incision after made a test of 100mg of intradermal ceftriaxone injection given slowly over 10 minutes. Group-2 consist of another 50 pregnant women who received the same dosage of antibiotic immediately after umbilical cord clamping. Those later groups' women were given test-dose 45 minutes before skin incision.

Post-operative follow-up was done looking for primary outcomes of febrile morbidity that diagnosed when temperature was > 38°C (100.4°F) on two-occasions 6 hours apart, excluding first 24 hours of delivery. This fever could be due to post-caesarean infection including; SSI that diagnosed with presence of purulent discharge, erythema and induration at incision site; endometritis that elicited if there is lower abdominal and/or uterine tenderness with tachycardia, leukocytosis, uterine subinvolusion, and foul-smelling lochia; UTIs

presented with positive urine culture(bacteriuria) with burning micturition and increased frequency of micturition.

When women's febrile morbidity was recognized, they underwent a thorough examination in order to identify the source of infection. The complete blood count and urine analysis were done. Women diagnosed with superficial-SSI were managed with only dressing, whereas those with deep-SSI were managed with re-suturing after dressing. Therapeutic-antibiotics were added with respect to culture sensitivity. All women were followed-up and discharged thereafter if no other complications occur. None of the women were lost to follow-up and all 100 mothers were analyzed in the study's groups.

Regarding secondary outcomes, neonatal sepsis was diagnosed clinically and para-clinically including clinical examination, blood picture, and positive blood-culture and C-reactive protein determined by neonatologist.

Concerning Ethical consideration, such study was approved by the Ethical Committee of Family and Community Medicine Department at Al-Iraqia Medical College. Official permissions were obtained from hospitals' administration and staff. Written informed consent were obtained from each woman and her in-charge relatives accompany with detailed explanation of study's purpose and importance and absolute confidentiality was reassured.

All recorded-data were entered and analyzed using SPSS version 25. Qualitative data were compared by Chi-square test. Quantitative data were compared using independent t-test. A P <0.5 was set significant for all tests.

Results

Out of 120 pregnant women enrolled, 100 were eligible after inclusion and exclusion criteria and randomized into two groups based on time they received single-dose ceftriaxone (50 women received 1-gram half to one hour prior to skin incision and another 50 immediately after cord clamping).

Regarding the demographic characteristics, both groups illustrated to have a non-comparable characteristics including; the age (27.84±0.370 vs. 27.70±0.463), gestational age (37.86± 0.351 vs. 37.72±0.454), and BMI (24.90±0.303 vs. 24.76±0.431) for group-1 and group-2 respectively (each P >0.05) (Table 1).

Table 1 Demographic characteristic of study's groups

Characteristic (mean± SD)	Group-1 (n=50)	Group-2 (n=50)	P-value	95% CI
Age	27.84± 0.370	27.70± 0.463	1.670* 0.098	-0.026–0.306
Gestational-age (Weeks)	37.86± 0.351	37.72± 0.454	1.727* 0.088	-0.021–0.301
BMI	24.90± 0.303	24.76± 0.431	1.878* 0.064	-0.008–0.288

* Values of independent t-test.

Similarly, those other characteristics related to women's parity and indications for caesarean-section were not statistically significant (each P>0.05) (Figure 1-3).

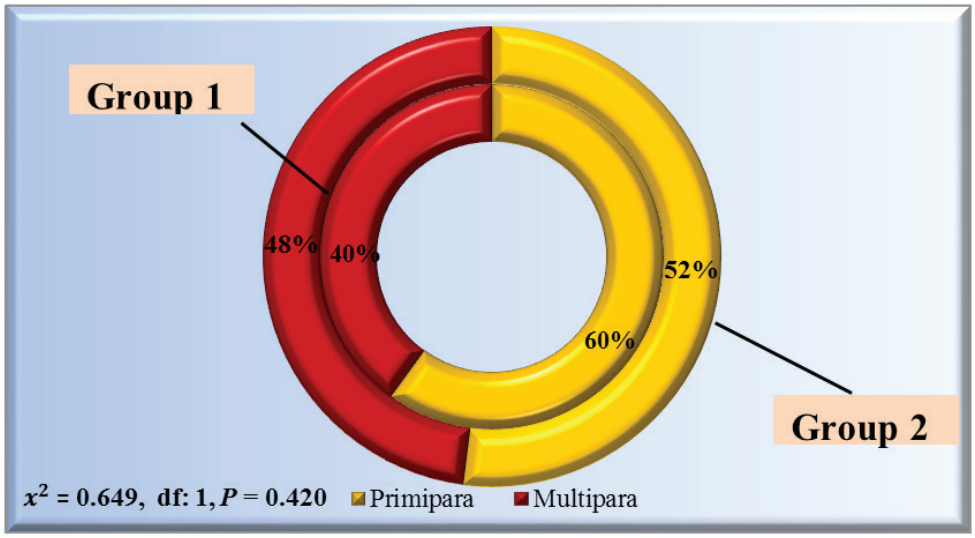

Figure 1 Distribution of maternal parity among study's groups

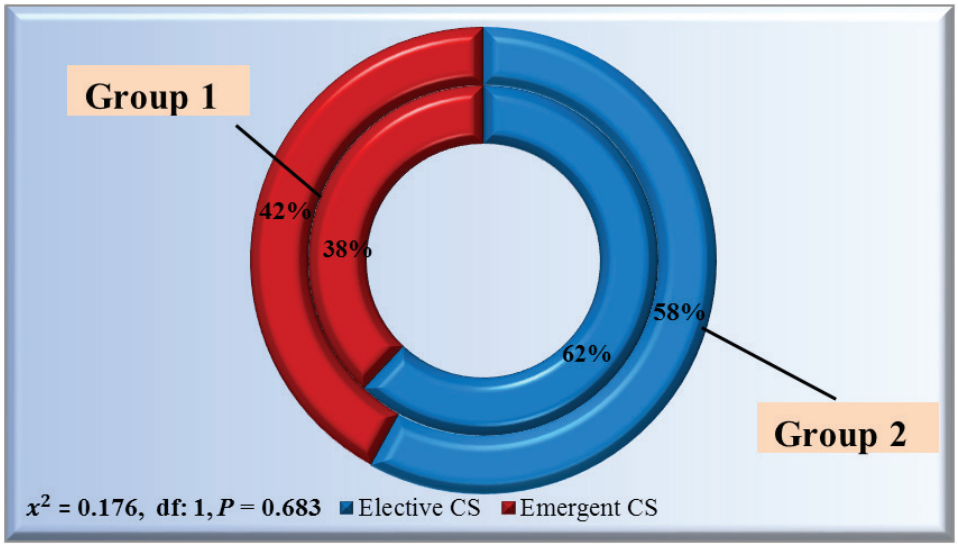

Figure 2 Distribution of caesarean-section among study's group

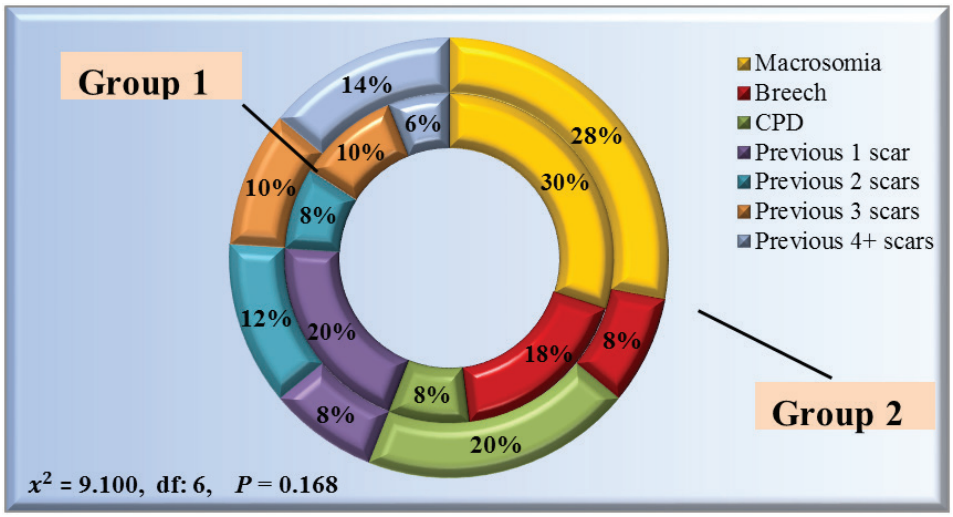

Figure 3 Indications for caesarean-section among study's groups

In respect to post-caesarean maternal outcomes, statistically significant differences were found among study's groups, where incidences of maternal febrile morbidity (fever from 2nd post-operative day) was higher among women in group-2 as compared to those whose in group-1 (20% vs. 6%) respectively($\chi^2\chi^2$:4.332, df:1, *P*=0.037). Likewise, the incidences of SSI (22% vs. 6%) ($\chi^2\chi^2$:5.316, df:1, *P*=0.021), wound dehiscence (18% vs. 2%) ($\chi^2\chi^2$:7.111, df:1, *P*=0.008), endometritis (16% vs. 4%) ($\chi^2\chi^2$:4.000, df:1, *P*=0.04), urinary tract infection (18% vs. 4%) ($\chi^2\chi^2$:5.005, df:1, *P*=0.025), and maternal hospital stay in-days (4.24± 0.431 vs. 3.14± 0.351) (t: 13.993, 95% CI:-1.256- 0.944, *P*=0.000) were significantly higher among group-2 women than those in group-1 respectively(Table 2).

Table 2 Post-caesarean infectious maternal outcomes among study's groups

Maternal Outcomes	Group-1 (n=50)		Group-2 (n=50)		Total (n=100)		P-value
	n	%	n	%	n	%	
Fever	3	6.0	10	20.0	13	13.0	4.332* 0.037
Surgical site infection	3	6.0	11	22.0	14	14.0	5.316* 0.021
Wound dehiscence	1	2.0	9	18.0	10	10.0	7.111* 0.008
Endometritis	2	4.0	8	16.0	10	10.0	4.000* 0.046
Urinary tract infection	2	4.0	9	18.0	11	11.0	5.005* 0.025
Hospital stay (mean ± SD)	3.14± 0.351		4.24± 0.431		13.993** (-1.256- -0.944)***		

* Values of Pearson Chi-square test.

** Value of independent t-test.

*** P value < 0.001

Concerning neonatal outcomes, there are no statistically significant differences among study's groups in relation to neonatal morbidities of neonatal fever, sepsis, poor-feeding, birth asphyxia and admission into neonatal intensive-care unit (each *P*>0.05) (Table 3).

Table 3 Post-caesarean neonatal outcomes among study's groups

Neonatal Outcomes	Group-1 (n=50)		Group-2 (n=50)		Total (n=100)		P-value
	n	%	n	%	n	%	
Neonatal fever	3	6.0	7	14.0	10	10.0	1.778* 0.182
Sepsis	3	6.0	8	16.0	11	11.0	2.554* 0.110
Poor feeding	4	8.0	6	12.0	10	10.0	0.444* 0.505
Birth asphyxia	4	8.0	8	16.0	12	12.0	1.515* 0.218
Neonatal intensive-care admission	6	12.0	13	26.0	19	19.0	3.184* 0.074

* Values of Pearson Chi-square test.

Discussion

This study identified a significant benefit of antibiotic administration in decreasing the incidences of maternal post-operative infectious morbidities in pre-incision group as compared to post-cord clamping group, where incidence rate of fever from second-day postoperatively was significantly lower in group-1 in comparison to group-2 and such finding is consistent with what was reported by Mandal *et al.*[4] showed that 5.4% vs. 21.5% of women who received antibiotic prior to incision and after cord clamping respectively developed fever two days postoperatively. Bhattacharjee *et al.*[11] revealed that 33% of the women of post-cord clamping developed post-operative fever as compared to 26% of those with fever in pre-incision group. Jyothirmayi *et al.*[12] reported that women of pre-incision group had significantly less febrile illness as compared with those who in the post-incision group. In contrast, Baaqaeel *et al.*[6], and Kalaranjini *et al.*[13] found that there were no significant differences regarding maternal febrile morbidity among women who received antibiotic either pre-incision or after cord-clamping.

Diagnosed surgical site infections were identified in 6% of women of pre-incision group as compared to 22% of those who in cord clamping group which are supported to what was reported by Mandal *et al.*[4] as 3.26% vs. 8.60% of women in comparable groups developed such complications respectively. Furthermore, the findings of Rai *et al.*[3], Bhattacharjee *et al.*[11], Jyothirmayi *et al.*[12] Kalaranjini *et al.*[13], and Brown *et al.*[14] were also supported. However, non-significant differences were reported by Baaqaeel *et al.*[6], and Witt *et al.*[10], that could be attributed to differences in applied research methods and designs.

Likewise, wound dehiscence found to be significantly comparable among our study's groups with higher incidence reported among post-clamping group, and such result is similar to what was reported by Rai *et al.*[3]. In contrast, Mandal *et al.*[4], Witt *et al.*[10] and

Bhattacharjee *et al.*[11] reported that wound dehiscence had insignificant difference among groups.

Endometritis incidences were significantly comparable among study's groups with lower rates observed in pre-incision group which is in line of other studies; Rai *et al.*[3], Mandal *et al.*[4], Baaqaeel *et al.*[6], Bhattacharjee *et al.*[11], and Jyothirmayi *et al.* [12]. However, contrary findings were reported by Austrian and Chinese studies of Witt *et al.*[10] respectively revealed no significant differences were found regarding postpartum Endometritis among study's groups.

Post-caesarean UTI found to have significant differences between study's groups as it was higher in post-cord clamping group than that in pre-incision and such findings are in concordance of what were reported by Rai *et al.*[3], and Jyothirmayi *et al.*[12]. Nevertheless, these findings are contrary to other studies; Mandal *et al.*[4], Witt *et al.*[10] and Kalaranjini *et al.*[13].

The mean hospital stay of mothers in present study was significantly higher in post-cord clamping group in comparison with pre-incision group which is consistently in the line of other studies; Mandal *et al.*[4], Bhattacharjee *et al.*[11], and Jyothirmayi *et al.*[12]. Contrariwise, non-significant results were found in study conducted by Witt *et al.*[10] in Austria.

In respect to neonatal outcomes, our study found that the neonatal fever, sepsis, poor-feeding, birth asphyxia and admission into intensive-care units had no significant differences between study's groups and these findings are supported by other studies; Rai *et al.*[3], Mandal *et al.*[4], Baaqaeel *et al.*[6], Bhattacharya *et al.*[11], Jyothirmayi *et al.*[12], Kalaranjini *et al.*[13].

Furthermore, the present study shows no significant difference among study's groups regarding demographic characteristics in relation to mean of women's age, gestational-age or their BMI as well as to the indications for caesarean-section whether in form of type or underlying causes that was also supported by other studies; Rai *et al.*[3], Mandal *et al.*[4], Bhattacharya *et al.*[11], Jyothirmayi *et al.*[12], and Brown *et al.*[14].

Conclusion

The administration of prophylactic antibiotic preoperatively significantly reduced the incidences of infectious maternal morbidities as compared with intraoperative administration as well as it lowers the incidences of adverse neonatal outcomes despite such differences did not attained statistical significance owing to constraints of small sample size in short span of study's conducted time. Thus the study emphasizes the need for further researches with a larger sample over long-duration to overcome the cautious interpretations resulted from power limitation of current study and achieves significant results.

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Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest**.**

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