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Risk Factors for Sepsis Following Cesarean Section in Ulaanbaatar: A Case-Control Study

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Objectives: The aim of this study was to determine the incidence of post-cesarean sepsis in patients undergoing a cesarean section (CS) and to identify risk factors and the impact of antibiotic prophylaxis on this condition. **Methods:** All cesarean deliveries performed at Ulaanbaatar Urguu Maternity Hospital and National Center for Maternal and Child Health (NCMCH) from October 1st 2013 to October 1st 2015 were evaluated for sepsis, based on criteria established by Centers for Disease Control and Prevention's National Healthcare Safety Network (CDC/NHSN). Medical records of case study and control patients were reviewed when they had post operation infection and revisited the hospital. Records were also compared to and included sociodemographic and clinical characteristics. **Results:** Overall findings were: 47.4% (361/ 761) of cases were complicated by wound infection and the control group without wound infections was 52.6% (400/761). Post-cesarean wound infection risk factors were statistically determined by: 1) emergency surgery (95% CI = 2.8; P = 0.35); 2) Twin pregnancy (95% CI = 5.8; P = 0.2); 3) Premature rupture of membrane (95% CI = 6.4; P = 0.26) and; 4) Failed induction (95% CI = 4.6; P = 0.5). **Conclusion:** Identifying high-risk patients who will require intensive postoperative care is critical in reducing incidences of post-cesarean wound infection.

Keywords: Cesarean Section, Risk Factors, Maternity Hospital, Wound Infection, Sepsis

Introduction

Post-cesarean sepsis following cesarean delivery is a major cause of morbidity and mortality thereby, increasing duration of patient hospitalization and hospital costs [1]. Given the short length of postoperative stay in the hospital [typically 2-4 days], the overall rate of infection following CS is likely to be significantly higher than UK postsurgical infection estimates [21]. Although, the causes of cesarean wound infection are similar throughout the world, with slight regional variations, the relative cause differs from region to region and from City Centre to City Centre [6]. The beneficial effect of antibiotic prophylaxis in reducing occurrences of infection associated with elective or emergency CS is well established [7]. Various factors affect infection rates in different settings. Those most frequently cited in medical journals include: 1) high maternal weight (underweight or obesity); 2) Prolonged

labor or rupture of membranes; 3) Long duration of surgery; 4) Multiple procedures; 5) Manual removal of placenta; 6) Young maternal age; 7) Maternal preoperative condition; 8) Procedure related blood loss; and 9) Absence of antibiotic prophylaxis [5].

Despite recent progress in developing a medical infrastructure in Mongolia, delivery of high-quality services with early interventions to reduce wound infections is an important aspect of patient safety procedures [10]. The occurrence, risk factors and distribution of pathogens isolated from post-CS sepsis at Ulaanbaatar Urguu Maternity Hospital and NCMCH are not known. Moreover, there is no evidence-based data to support preoperative and postoperative care protocols at these hospitals. Therefore, this study was done to determine the incidence, susceptibility pattern of the isolates and factors associated with post-cesarean sepsis among women undergoing CS at Urguu Maternity Hospital and National Center for Maternal and Child Health.

Materials and Methods

1. Subjects

Patients were serially [voluntarily] enrolled until the sample size was reached. The sample size was calculated using the retrospective study as an examination for specific factors associated with post-cesarean wound infection classified as either having wound infection in patient case studies or no wound infection in control patients [16]. The occurrence rate used was the rate of post-cesarean wound infection among patients with skin incision transverse and vertical [11]. The minimum sample size obtained was 721, but the study enrolled 800 pregnant women. The inclusion criteria for enrollment in the study were patients who underwent CS and had a diagnosis of post-cesarean sepsis within 30 days of the obstetric procedure. A routine of infection control evaluated all patients who had a CS until 30-days after the procedure. Control patients were determined after the inclusion of case study patients and according to the following inclusion criteria: similar age (±2 years), CS procedure performed on the same day as the case study patient, no history of post-cesarean infectious complication up to the 13th day and taking into account the CDC/NHSN criteria [19]. Cases were excluded if a control patient meeting the inclusion requirements could not be specifically identified or if patient records were not available. Medical records of case study patients and control patients were reviewed with respect to sociodemographic characteristics, elective or emergency cesarean, comorbidities, duration of labor, use of appropriate antibiotic prophylaxis and duration of membrane rupture, the number of internal vaginal examinations, and length of hospitalization. An appropriate prophylaxis was typically defined before the antibiotic was administered—within 30–60 min before the procedure.

2. Methods

The study was conducted during the period of October 1st 2013 to October 1st 2015 in 2 maternal hospitals in Ulaanbaatar; Urguu Maternity Hospital and National Center for Maternal and Child Health,. These hospitals were randomly selected from Ulaanbaatar City. All samples selected from CS operations were intended to achieve the goals of these studies that if surgeon technique or antibiotic prophylactic become incidence. Up to and post operation surveys followed patients until 30-day after the operation. 47.4% (361/ 761) of cases were found to be complicated with wound infection and the control group without wound infection was 52.6% (400/761). CS was performed after an agreed protocol and through Pfannenstiel incision. Those patients who received a vertical lower segment CS were interviewed after they visited the hospital for post-CS examination. Women who had a CS via a midline sub umbilical vertical skin incision were excluded from the patient study analysis as per protocol.

3. Data Analysis

Statistical analysis was performed using a descriptive evaluation with the mean ± standard deviation for continuous variables and frequency and percentage for categorical variables. The Student's t-test for independent samples was used for comparing the means between groups and a chi-square test to compare categorical variables. Those variables associated with the outcome in univariate analysis with a significance level below 0.2 were included in a multivariate logistic regression model. The odds ratios between factors and outcomes of their respective 95% confidence intervals were calculated. Also, a stepwise backward multiple regression was performed to reveal the best set of predictors of post-cesarean wound infection. Microsoft Excel software was used for the data storing and analyses were performed using SPSS for Windows.

4. Post-cesarean wound infection and sepsis

CDC reports state that post-cesarean wound infection should be suspected within 30 days of a surgical procedure if at least one of the following symptoms are present: localized swelling, with or without purulent discharge from the wound, pain or tenderness, redness, malodor or fever.

5. Details of ethics approval

Ethical approval was obtained from Ethical Committee meeting №10/1A of the School of Medicine, Mongolian National University of Medical Sciences on 11th April 2011. Each patient's medical record was checked and selected patients signed a consent form provided by related doctors before being involved in the study.

Results

During the 2 year study, seven hundred twenty one consenting women scheduled for CS and having met the inclusion criteria of CDC/NHSN were enrolled in the study. Three hundred sixty one cases meeting the inclusion criteria experienced wound infection. Four hundred subjects who did not experience post-cesarean wound infection served as the control group Table 1. Data presented in Table 1 suggests there is evidence that post-cesarean wound infection obstetrics are symptoms of Premature rupture of Membrane or Prolonged operation time. Anemia rates are not independent of whether a sample is predominantly in a case group or predominantly in the control group (χ^2=0.165-5.294; p=0.0073). However, there is significant statistical evidence regarding age of the patient with case and control groups (χ^2=0.041-1.393;p=0.0073). The characteristics of the 361 case patients and 400 control patients are described in Table 2. The factors that differentiated case study patients from control patients in the logistic regression analysis for univariate analysis were performed and significant risk factors from emergency surgery (95% CI = 2.8; P = 0.35), twin pregnancy (95% CI = 5.8; P = 0.2), premature rupture of membrane (95% CI = 6.4; P = 0.26), failed induction (95% CI = 4.6; P = 0.5) and also non-significant risk factor for prolonged operation time (95% CI = 1.12; P = 0.036).

Predictors of post-cesarean sepsis

Univariate analysis indicated, post-cesarean sepsis occurs significantly more often among women with: wound infection prior to surgery (HR = 2.7; 95% CI = 1.4-5.5; P = 0.005), prolonged duration of operation (a surgical procedure lasting longer than 1 hour) (HR = 2.4; 95% CI = 1.1-5.0; p = 0.020), and a procedure performed by an intern or junior doctor (HR = 2.8; 95% CI = 1.3-6.1; p = 0.012) (Tables 3). These results indicate that sampled case study patients' surgery technique may not be related to the actual technique itself but to other risk factors that affect evaluation of post-cesarean wound infection. However, the following factors had no effect on the occurrence of post-cesarean wound infection: age, gravidity,

Table 1. Case and control group obstetric clinical characteristics of patients undergoing CSs, with and without subsequent cesarean wound infection among women

Variable	Cases N = 361(%)	Controls N = 400(%)	Cases x^2 test	Control x^2 test	p-value
Maternal age					
less than 19	135(37.3)	180(45)	1.393	1.257	0.0739*
20-39	25(6.9)	30(7.5)	0.045	0.041	
Greater than 40	201(55.6)	190(47.5)	1.298	1.171	
Premature rupture of membrane	9 (2.5)	29(7.2)	0.769	0.165	0.0073
Prolonged operation time	7 (2)	10(2.5)	5.294	1.138	
Anemia	4(1)	54(13.5)	3.824	0.822	

*x^2 test – Age was significantly affected through the post-cesarean wound affection.

Table 2. Univariate analysis of preoperative risk factors for wound infection in patients who underwent CSs

Predictive factors	Post-cesarean wound infection			
	Yes (n = 361)	No (n = 400)	OR (95% CI)	p-value
Age in years				
less than 19	135	180	3.5	0.001
20-39	25	30	10.2	0.211
Greater than 40	201	190	1.16	0.049
Childbearing 2-4 times	16	27	0.4	0.23
Childbearing 5-8 times	22	20	2.3	0.03
Emergency surgery	12	7	2.8	0.35
Twin pregnancy	27	13	5.8	0.2
Premature rupture of membrane	31	18	6.4	0.26
Failed induction	12	7	4.6	0.5
Pyelonephritis	23	15	2.4	0.42
Anemia	4	1	3.7	0.32
Prolonged operation time	56	35	1.12	0.036

parity, gestational age at delivery, anemia, preoperative length of stay, timing of antibiotic prophylaxis or the amount of blood loss intraoperatively.

After adjustment for confounders of age and childbearing status (Table 4), only 3 variables retained significant association with post-cesarean wound infection. These variables are: 1) prolonged latent phase (OR 1.5); 2) premature rupture of membrane (OR 12.5); and 3) failed induction of labor (OR 3.7). Multivariate analysis did not include factors with high collinearity such as; ASA and duration of rupture of membrane. The independent risk factors for post-cesarean sepsis were identified in this study by multivariate Cox regression analysis were contaminated wound (HR = 2.5; 95% CI=1.2-5.1; p = 0.016), multiple vaginal examinations (HR = 2.6; 95% CI=1.3-5.3; p = 0.008) and an operation performed by an intern or junior doctor (HR = 4.2; 95% CI=1.8-9.5; p = 0.030) (Table 4). These results indicate that operations carried out by an intern or junior doctor and prolonged duration of the surgical procedure are independent factors, which increase the risk of post-cesarean sepsis—at minimum according to this study.

Antibiotics administered during this study can be divided into 2 groups: cefazolin based regimen and non cefazolin regimen (Table 4). The timing of antibiotic administration was not consistent. In contrast to these studies, no significant difference was observed compared to previous studies [20] regarding type of antibiotic prophylaxis and post-cesarean wound infection.

Discussion

The current study's incidence of post-cesarean wound infection (47.4%) is much higher than the 23.4% reported by Makinde from Ile-Ife Nigeria [11]. It is important to state that although the current studies' results of 47.4% is near to worldwide reported incidence ranges by Moir–Bussy et al. in a hospital survey performed in London, it is much higher than figures reported by most developed countries [14, 13]. If we compare our cases with reports from developed countries, our studies case (47.7%) is higher but the previous study was perhaps too old to be reasonably comparative to recent data [1-3]. However, it highlights the facts that with the use of standardized protocols and good practices, it is possible to reduce cesarean wound infection from the high rate of (47.5%) in Ulaanbaatar to Nigeria's 23.4%. Previous studies investigated associations between; maternal age, anemia, prolonged labor and post-cesarean wound infection [3-15]. Findings indicate that wound infection due to anemia is likely to occur in severe conditions and

Table 3. Univariate analysis of intraoperative risk factors for wound infection among patients who underwent CSs

Predictive factors	Post-cesarean wound infection		OR (95% CI)	p-value
	Yes (n = 361)	No (n = 400)		
Wound class				
Clean and contaminated clean	100	240	1.0	
Contaminated and dirty	261	160	2.7 (1.4-5.5)	0.005
Type of skin incision				
Vertical	361	400	1.1-11.8	0.034
Duration of procedure in mins				
≤60	162	301	1.0	
>60	199	99	2.4 (1.1-5.0)	0.02
Type of surgeon				
Senior*	170	250	1.0	
Junior**	191	150	2.8 (1.3-6.1)	0.012
Estimated blood loss in mls				
≤500	250	259	1.0	
>500	111	141	1.4 (0.6-2.9)	0.436
Antibiotic used				
Non Cefazolin regimen	160	198	1.0	
cefazolin regimen	201	202	1.4 (0.7- 2.8)	0.304
Duration of antibiotic course				
Single dose	45	105	0.8 (0.4-1.8)	06.08
Multiple dose	316	295	1.0	

*Senior doctor included postgraduate student, registered medical doctor and specialist.
**Junior surgeon defined an intern doctor.

Table 4. Multivariate Model of risk factors for wound infection in patients who underwent CSs

Independent risk factor	OR (95% CI)	p-value
Prolonged latent phase	1.9	0.2
Premature rupture of membrane	7.2	0.26
Failed induction of labor	12.3	0.5
Contaminated wound	2.5 (1.2-5.1)	0.016
Multiple vaginal examinations	2.6 (1.3-5.3)	0.008
Operation done by Intern doctor	4.2 (1.8-9.5)	0.03
Severe anemia (Hb <7 g/dl)	3.8 (1.2-12.4)	0.028
Duration of procedure >60 minutes	2.3 (1.1-4.8)	0.03

OR- Odds Ratio, CI - Confidence Interval

not in mild cases. This was not a surprise. The majority of our case study patients were in the "severe condition." Good homeostatic techniques may reduce incidence of hematoma collection leading to wound infection. In the present study, 18.95% of Escherichia coli isolates were resistant to Ciprofloxacin, and gentamicin; similar to the findings of Fantahamu et al. [6]. The rate of resistance to these antibiotics was higher than the rate of resistance to ampicillin and erythromycin. Resistance to antibiotics may be the result of "self-

prescription" in the community. Various risk factors were found to predict post-cesarean wound infection [14, 13]. One factor is the young maternal age of the patients. An association was recorded between maternal age and post-cesarean sepsis, suggesting women aged 30 years or younger were more likely to have a post-cesarean wound infection than those over 30 years in age [2, 17]. Despite this trend, the association was not proven to be statistically significant ($p = 0.055$). In accordance with previous studies, an ASA physical status classification score of 3 or more was found to significantly predict post-cesarean wound infection ($p = 0.005$), which is in agreement with previously reported findings [17, 19]. Prolonged labor (≥12 hrs), prolonged rupture of membranes (≥8 hrs) and multiple vaginal examinations (≥4 times) were significant predictors of post-cesarean wound infection in this study, which are in agreement with previously obtained results [8, 14, 17]. Normally during pregnancy, cervical mucus plug, fetal membranes and amniotic fluid all serve as barriers to infection. However, when the membrane is ruptured, this protective effect is gradually reduced as amniotic fluid loses its sterility. It is thought that the non-sterile amniotic fluid may act as a transport medium by which bacteria come into contact with the uterine and skin incisions leading to chorioamnionitis.

Another important risk factor for post-cesarean wound infection is the absence or delay of antibiotic prophylaxis. In this study, there was no standard policy of antibiotic prescription. Generally, Mongolia often uses a choice of antibiotics which are administered depending on the particular surgeon and indication of CS.

In the present study, operations performed by an intern or junior surgeon increased the risk for post-cesarean wound infection 4 fold, as shown by multivariate analysis. This could be explained by the fact that a majority of junior surgeons who made a vertical incision in the abdominal wall had less experience in handling the tissue, controlling blood loss, and as a result, the procedures were prolonged longer than 1 hour [6].

Hypertensive disorders of pregnancy, contaminated wound, multiple vaginal examinations, operations carried out by an intern or junior doctor and prolonged duration of the surgical procedure (Longer than 60 minutes) have been found to be independent factors which increase risk of post-cesarean wound infection at Ulaanbaatar City Maternal Hospital and National Center for Maternal and Child Health. Identifying high-risk patients who require intensive postoperative care is critical for reducing incidences of postcesarean wound infections. This can be achieved if independent risk factors for post-cesarean wound infection are well understood within the clinical setting.

Limitations: There are several limitations inherent in this study. First, Our research team followed scientific research ethics that require researchers to select only patient volunteers and provide compensation to them. Therefore, before the CS operation we selected samples from each volunteer and informed them that the cost of their CS cost will payed by our team. Unfortunately, we were not able to cover all CS operations due to our limited budgets. As a result, we were only able to sample the limited number of CS cases as shown in this study. Perhaps, for this reason our study case control group does not compare well with other studies. Second, with regard to CS specific variables that were chosen, for wound infection, there were myriad variables that measure long-term firm performance. The variables used in this study were selected for ease of data gathering. Other variables may be better independent risk factors of the relationship between care of patient and skill performance. Third, the change in surgeons was not considered. It is probable that for at least some of the surgical operations, surgeons were changed for specific patients during the 2-year study period. As surgeons change, it is likely that risk of post cesarean wound infection also changes. Perhaps, patients with experienced surgeons have less wound infections than patients with surgeons with limited experience. If this is true, changes in surgeons with more experience may reduce risk of infection.

Our study did not estimate if CS is unnecessary or a necessary surgery for mother and child. However, we were able to predict exact causes of main risk factors that are necessary for CS instruction. Therefore, future investigators should identify this issue regarding our main risk factors study.

In conclusion, hypertensive disorders of pregnancy, contaminated wound, multiple vaginal examinations, CS operations carried out by an intern or junior doctor and prolonged duration of the surgical procedure have been found to be independent factors which increase the risk of post-cesarean sepsis in the present study. Post-cesarean wound infection independent risk factors were statistically determined as being: the prolonged latent phase, premature rupture of membrane and failed induction of labor. All upper independent risks should be utilized in designing wound infection prevention and control strategies. Good homeostatic technique may reduce the incidence of hematoma, which leads to wound infection. Identifying high-risk patients who require

intensive postoperative care is critical for reducing the incidence of post-cesarean wound infection. Prophylactic antibiotics should be the standard of care in cases complicated by any of these factors.

Conflict of Interest

The authors state no conflict of interest.

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