

The Prevalence, Risk Factors, and Bacterial Profile of Cesarean Surgical Site Infections at a University Teaching Hospital in South Western Uganda

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Abstract

Introduction: The single most important risk factor for post-partum maternal infection is Cesarean section (C/S) with a 5-20-fold greater risk for infection compared to a vaginal delivery. Post Cesarean wound infection is diagnosed in 2.5 to 16 percent of patients. Early wound infections (in the first 24 to 48 hours) are usually due to group A or B beta-hemolytic streptococcus and are characterized by high fever and cellulitis while later infections are likely due to *Staphylococcus epidermidis* or *aureus*, *Escherichia coli*, or *Proteus* species.

Objectives: To determine the prevalence, risk factors and bacterial profile of wound sepsis following Cesarean at Mbarara Regional Referral Hospital (MRRH).

Methods: A cross sectional study of mothers who delivered by Cesarean at MRRH was conducted. Mothers were recruited consecutively until the sample size was achieved. The main dependent variable was wound sepsis confirmed by a positive culture for microorganisms.

Results: Of the 359 mothers recruited in the study, 54 (15.5%) developed Cesarean wound sepsis. The risk factors associated with post Cesarean wound sepsis were severe anemia, lack of preoperative antibiotics use, poor antenatal attendance, mothers referred from peripheral health facilities, abnormal Body Mass Index (BMI), diabetes mellitus, more than five vaginal examinations, prolonged rupture of membranes before C/S, and prolonged labour. *Staphylococcus aureus* was isolated in 48.2% of all the septic cases and most of the bacterial isolates were susceptible to ceftriaxone, ceftazidime, ciprofloxacin and nalidixic acid and resistant to penicillin.

Conclusion: The prevalence of post Cesarean wound sepsis is high with *staphylococcus aureus* being the most common bacteria isolated in infected wounds. Most of the bacteria were susceptible to third generation cephalosporins and quinolones. Antibiotics use was protective against developing wound sepsis.

Keywords: Uganda, Bacterial Profile, Susceptibility Patterns, Factors

Background

The clinical criteria used to define a primary superficial surgical site infection (SSI) include any of the following: a purulent discharge within 30 days from the superficial surgical site, organism isolated from an aseptically obtained culture of fluid or tissue from the superficial incision, the surgeon's diagnosis of infection and a surgical site that requires reopening by the Surgeon and is culture positive or not cultured but patient has at least one of the following signs or symptoms; pain or tenderness, localized swelling, redness or heat (CDC, 2013). The rates of Cesarean SSIs in sub-Saharan Africa vary between 9-33% [1-4]. Women giving birth by Cesarean section

have a 5- to 20-fold greater risk of postpartum sepsis than women giving birth vaginally [5]. The commonest post-delivery infections are endometritis (puerperal sepsis), surgical site infections (SSIs) and wound infections [6,7]. Postpartum sepsis is the commonest cause of maternal mortality at Mbarara Regional Referral Hospital (MRRH) in Uganda, causing 31% of all maternal deaths [8]. Independent risk factors for post caesarean SSIs include hypertensive disorders of pregnancy, contaminated wound, prolonged duration of operation and an operation performed by an intern or junior doctor [9].

Surgical site infections can be prevented by giving prophylactic antibiotics and strict adherence to antibiotic prophylaxis and infection control guidelines can reduce postpartum sepsis incidence by 70% [5]. Implementation of evidence-based measures such as

prophylactic antibiotic administration before Cesarean section significantly reduces surgical site infections and as thus women undergoing Cesarean section should receive the prophylactic antibiotics [10,11]. Intravenous prophylactic antibiotics for Cesarean section given preoperatively compared with administration after cord clamp significantly reduces the incidence of surgical site infections [11]. World Health Organization (WHO) recommends use of pre-Cesarean delivery prophylactic antibiotics 30 to 60 minutes prior to operative skin incision to reduce the risk of postoperative infection [11-14]. We therefore set out to evaluate the prevalence, bacterial profile and risk factors of wound sepsis following caesarean section at Mbarara Regional Referral hospital.

Methods

Study Setting and Design

The study was a cross-sectional and 341 participants were recruited from Mbarara Regional Referral Hospital (MRRH) in Mbarara, Uganda. MRRH is an approximately 650-bed academic hospital affiliated with Mbarara University of Science and Technology (MUST). The current hospital policy is for women delivering by Cesarean to receive a single dose of pre-operative antibiotics (ampicillin or ceftriaxone), usually given within 30 minutes to one hour of skin incision. In addition, after Cesarean section women are treated with combination intravenous ceftriaxone and metronidazole for three days, followed by five days of oral cefixime. Microbiological evaluation of potential infections is not routine, but when requested, samples are processed at MUST's teaching lab adjacent to MRRH [15]. For this study, wound sepsis was defined by a positive culture of fluid or tissue from the superficial incision for microorganisms.

Inclusion and Exclusion Criteria

All mothers who delivered by Cesarean and admitted on Maternity ward at MRRH were recruited into the study. Mothers who delivered by Cesarean at MRRH in postnatal ward from 3rd post-operative day till 30 days' post-surgery and those readmitted on gynecology ward with Cesarean wound complications within one-month post-surgery were included into the study.

Sampling Procedure

Consecutive sampling method was used to enroll all mothers who met the inclusion criteria until the sample size was achieved; this was done daily in postnatal and gynecology wards. Patients were strictly recruited once. To avoid double entry, each participant was assigned a unique identification number and sticker on her medical documents.

Sample Collection

We obtained wound swabs, urine, blood, vaginal discharge swabs for the various laboratory tests from the mothers who were recruited into the study.

Data Collection

A pretested questionnaire was administered to the study participants by the principle investigator or research assistant after obtaining consent to the study. The questionnaire captured information including socio demographic characteristics, medical and obstetric characteristics. Through swabbing the infected wounds, we isolated and identified bacterial pathogens responsible for wound infections through microbiological laboratories. Antimicrobial susceptibility profile of the bacterial isolates was determined by disk diffusion

Laboratory Procedures

This was assessed by collecting exudate from wounds by use of swabs. The swabs were transported at room temperatures to the laboratory as soon as possible. Swabs were inoculated on chocolate, blood and MacConkey agar. Chocolate plate was placed in a candle jar and incubated it with other plates at 35-37°C for 24-48 hours. An additional blood agar plate was inoculated anaerobically at 35-37°C for 48-72 hours. Plates were examined aerobically for potential pathogens like *Staphylococcus aureus*, beta Hemolytic streptococci, Enterobacteriaceae, *Pseudomonas aeruginosa*, *Acinetobacter* species, *Haemophilus influenzae*, and *Streptococcus pneumoniae*. Anaerobes were also investigated from the plates that were prepared anaerobically.

Drug Susceptibility Testing Using Kirby Backer Technique

For antimicrobial sensitivity patterns, agar plates were uniformly seeded with a suspension of fresh isolates of bacteria of the same colony per plate. Antimicrobial discs of the right potency were then aseptically placed on the plate which was then incubated in a suitable growth environment overnight. Zones of inhibitions were measured in millimeters. The sensitivity was interpreted according to the inhibition zone sizes as sensitive, intermediate and resistant.

Study Variables

The dependent variable was wound sepsis following Cesarean at MRRH. The independent variables were maternal age, parity, education level, marital status, occupation, religion, parity, antenatal care attendance, number of vaginal examinations, BMI, Use of pre-operative antibiotics, duration of rupture of membranes, presence of diabetes mellitus, indication for Cesarean, type of Cesarean, level of surgeon, referral status, presence of urine tract infection, HIV status, district of residence, HIV status, labour duration, surgical technique, indication for Cesarean, diabetes mellitus.

Statistical Analysis

Data was entered an Epi-Info version 7 and analysed using State version 11. A descriptive analysis for mean, median and proportions of the study population was conducted. The proportion of those with wound sepsis was estimated to determine the prevalence of wound sepsis in the study. Pearson chi-square χ^2 , logistic regression analyses were applied to determine associations. Odds ratios were used to determine the strength and direction of association. A p-value of less than 0.05 was considered significant.

Ethical Considerations

Institutional consent was sought from the department of Obstetrics and Gynecology and the Faculty Research Ethical Committee at Mbarara University of Science and Technology.

Results

The overall mean age for the study participants was 24.6 years. Most of the septic cases were in the group of 20-34 years (44) contributing to about 81.7% of all the septic cases. Rural residents contributed most of cases (70.4%) compared to their urban counterparts. The overall HIV prevalence in the study population was 11.7%. Majority of mothers who did not receive preoperative antibiotics had wound sepsis (88.9%) (Table 1). There were four types of micro-organisms isolated in the septic wounds following Cesarean during this study (*staph aureus*, *klebsiella*, *E. coli* and *proteus*). *Staphylococcus aureus* was the most prevalent accounting for 48.2% of the isolated microorganisms (Table 2). Amoxicillin, ampicillin, septrin and

chloramphenicol did not have therapeutic antibiotic activity on *Staphylococcus aureus* (Table 3).

Table 1: Participants' socio-demographic, obstetric and medical characteristics

Variable	Presence of infection, n	Absence of infection, n
Age		
<20	08	50
20-34	44	227
35-49	02	18
HIV Positive	04	37
HIV Negative	50	258
Urban	16	75
Rural	38	220
Married	23	103
Separated	02	02
Single	25	190
Primipara	22	97
Multiparous	25	25
Grand multipara	7	34
No education	6	28
Primary	26	152
Secondary	17	93
Post-secondary	05	22
More than 4 ANC attendance	37	210
Less than 4 ANC attendance	17	85
Referred	28	134
Not referred	26	161
No. of vaginal exams before Cesarean		
<4 times	23	236
≤4 times	31	59
Pre-operative antibiotics given	48	243
Pre-operative antibiotics not given	6	52
History of PROM	5	8
No history of PROM	49	287
Elective Cesarean	3	11
Emergency Cesarean	51	284
History of DM	4	2
No history of DM	50	293
BMI: Underweight	0	1
Normal	08	88
Overweight	42	115
Obesity	04	91

BMI-Body Mass Index; UTI-urinary tract infection; DM-diabetes

mellitus; C/S-Cesarean section; PROM- Prolonged rupture of membranes; ANC-antenatal care; HIV-human immuno-deficiency virus.

Table 2: Microorganisms isolated from the infected wounds

Organism isolated	Frequency n (%)
Staph aureus	27 (48.2)
Klebsiella	15 (26.8)
Escherichia coli	4 (7.1)
Proteus species	10 (17.9)
Total	56 (100)

Table 3: Antimicrobial resistance patterns for (*Staphylococcus aureus*)

Drug tested	% Resistance
Ampicillin	100
Amoxicillin	100
Gentamycin	0.0
Penicillin G	77.8
Chloramphenicol	100
Erythromycin	66.7
Septtrin	100
Augmentin	14.8
Oxacillin	77.8
Ceftriaxone	7.4
Ceftazidime	11.1
Tetracycline	85.2
Cloxacillin	51.9

There was marked resistance of the three isolated gram-negative micro-organisms against the following antibiotics: Chloramphenicol, septrin, tetracycline. Ciprofloxacin is still very potent towards the three micro-organisms (Table 4). After adjusting for cofounders, the factors associated with wound sepsis were the following: severe anemia (aOR 11.64, 95% CI 5.2-26.1, $P<0.001$), more than four vaginal exams before Cesarean (aOR 7.39, 95% CI 3.3-16.5, $P<0.001$), ruptured membranes for over 24 hours (aOR 9.89, 95% CI 2.1- 47.6, $P<0.001$), diabetes mellitus (aOR 8.70, 95% CI 3.9-19.3, $P<0.001$), being referred to Mbarara Hospital (aOR 3.98, 95% CI 1.7-9.4, $P<0.001$), prolonged labour (>18 hours) (aOR 6.06, 95% CI 2.6-14.3, $P<0.001$), antenatal care (ANC) attendance less than 4 times (aOR 2.11, 95% CI 1.1-4.2, $P=0.03$), abnormal body mass index (aOR 2.45, 95% CI 1.1-5.6, $P=0.03$). Receiving pre-operative Cesarean antibiotics was found to be protective against wound sepsis (aOR 0.38, 95% CI 0.17- 0.74, $P=0.01$) (Table 5 and 6).

Table 4: Antimicrobial resistance patterns for gram negative organisms

Drug	% Resistance for Klebsiella	% Resistance for E. coli	% Resistance for proteus species
Gentamicin	26.7	0.0	10.0
Chloramphenicol	86.7	100	100
Septin	93.3	100	90.0
Augmentin	13.7	0.0	0.0
Ceftriaxone	6.7	0.0	20.0
Ceftazidime	20.0	0.0	20.0
Tetracycline	100	100	100
Ciprofloxacin	0.0	7.4	0.0
Nalidixic acid	13.7	25.0	30.0

Table 5: Bivariate analysis of socio-demographic, obstetric and medical profiles of participants

Variable	cOR	95% CI	P value
Age in years:			
20-34	1.00		
>20	1.21	0.54-2.13	0.64
<34	0.69	0.13-3.61	0.66
HIV Positive	0.88	0.35-2.22	0.79
Residence status			
Urban dwellers	1.00		
Rural dwellers	0.81	0.43-1.54	0.52
Education Level:			
None	1.00		
Primary	0.79	0.30-2.12	0.65
Secondary	0.85	0.31-2.38	0.76
Post-secondary	1.42	0.28-3.98	0.93
Marital Status:			
Married	1.00		
Separated	4.48	0.59-33.45	0.14
Single	3.19	0.93-10.98	0.07
Parity: Multiparous			
Primiparous	1.49	0.79-2.79	0.21
Grand multiparous	1.35	0.54-3.38	0.52
Antenatal care attendance			
More than 4 ANC attendance	1.00		
Less than 4 ANC attendance	2.72	1.47-5.04	<0.001
Type of Cesarean done			
Elective Cesarean			
Emergency Cesarean			
Pre-operative antibiotics			
Pre-operative antibiotics	1.00		
Pre-operative antibiotics given	0.28	0.08-0.92	0.03

Type of skin closure			
Interrupted skin closure	1.00		
Subcuticular skin closure	1.41	0.55-3.63	0.48
Referral status			
Referred	0.29	0.14-0.58	
Not referred	2.12	1.16-3.91	0.01
No. of antenatal attendances			
<4 times	5.39	2.84-10.25	
≤4 times	3.16	1.71-5.83	0.04
Hb level below 7g/dl	7.97	0.20-42.50	<0.001
No. Vaginal exams: ≤5	5.39	2.84-10.25	<0.001
Prolonged labour (over 18 hours)	3.5	1.90-10.7	<0.001
Abnormal Body Mass Index	2.21	0.99-4.92	0.05

ANC-Antenatal Care; Hb-Hemoglobin; cOR-crude odds ratio; CI-confidence interval; C/S-Cesarean section.

Table 6: Factors associated with post Cesarean wound sepsis (Multivariate analysis)

Variable	aOR	95% CI	P-value
Abnormal body mass index	2.45	1.08-5.57	0.03
Diabetes mellitus	8.70	3.93-19.25	<0.001
ANC attendance less than 4 times	2.11	1.05-4.20	0.03
Above four vaginal exams before Cesarean	7.39	3.32-16.52	<0.001
Pre-operative antibiotics use	0.38	0.17- 0.74	0.01
Referred to MRRH	3.98	1.69-9.38	<0.001
Severe Anemia (Hb below 7g/dl)	11.64	5.19-26.08	<0.001
Prolonged labour (>18 hours)	6.06	2.58-14.27	<0.001
Prolonged rupture of membranes (>24 hours)	9.89	2.05- 47.61	<0.001

ANC-Antenatal Care; MRRH-Mbarara Regional Referral Hospital; Hb-Hemoglobin; aOR-adjusted odds ratio; CI-confidence interval; C/S-Cesarean section.

Discussion Prevalence

The prevalence of Post-Cesarean wound sepsis in our study was 15.5%. Other studies have found prevalence in the ranges of 2.5-33.3% [3,4,16,17]. The prevalence found in our study lies within the ranges like studies done elsewhere in sub-Saharan Africa because of similarities in population characteristics. The differences in the proportion figures arises from the differences in the study designs. Whereas our study was a cross-sectional study, some other studies

such as the one by Koigi and colleagues were longitudinal studies that determined incidence of wound sepsis [3].

Bacterial Isolates and Microbial Sensitivity Pattern

The commonest micro-organisms isolated in our study were *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli* and proteus species. Other studies done in sub-Saharan Africa also isolated similar micro-organisms such as *S. aureus*, *E. coli*, *Klebsiella pneumoniae*, *coagulase negative staphylococcus*. *S. aureus* has been isolated as the most prevalent micro-organism [2,15,18,19]. In our study, there is high sensitivity to cephalosporins and quinolones and wide spread resistance to penicillin such as ampicillin. This is comparable to other study findings [18]. This may be attributed to the irrational use of commonly available antibiotics within the low resource settings. The populations studied are similar in their characteristics, hence the near similarities in the micro-organisms isolated and the antimicrobial susceptibility patterns.

Risk Factors

The risk factors found in our study were severe anemia, more than four vaginal exams before Cesarean, and ruptured membranes for over 24 hours, diabetes mellitus, being referred to Mbarara Hospital, prolonged labour, antenatal care (ANC) attendance less than 4 times, and abnormal body mass index. Some studies have also found the following as risk factors wound sepsis: abnormal body mass index (BMI), hypertensive disorders, premature rupture of membranes, diabetes mellitus, emergency Cesarean delivery [2,4,20,21]. Mothers with anemia were more likely to have wound sepsis because a higher concentration of Hemoglobin helps in the oxygen carrying capacity of blood and thus severe anemia therefore hinders wound healing and immunity because of poor oxygen carrying capacity. Prolonged rupture of membranes predisposes to wound infection because when there is prolonged rupture of membranes, there is a chance of ascending infection and chorioamnionitis and wound infection may supervene following Cesarean.

Mothers with diabetes mellitus are more prone to development of wound compared to their normal counterparts because hyperglycemia impairs neutrophil function there by reducing the immunity of the mothers. The reduced immunity will predispose mothers to secondary infections. Also due to peripheral arterial disease caused by diabetes mellitus, reduced blood supply to the wound will impair healing and immunity there by predisposing the wound infections [22]. Mothers who were in labour for over eighteen hours were more likely to develop wound sepsis due to factors such as early rupture of membranes and multiple vaginal examinations which could lead to ascending infections leading to chorioamnionitis which in turn leads to infection of the post Cesarean wounds [2]. The mothers who had more than four vaginal examinations in labour were more likely to develop wound sepsis due to enterococci contamination from the anorectal region leading to ascending infection of liquor [23].

Pre-operative antibiotics use for Cesarean was found to be protective against development of post Cesarean wound sepsis. Administration of pre-operative antibiotics within 30 to 60 minutes of skin incision reduces risk of postoperative infection by almost 70% and maximizes concentrations at the surgical site [5,11-14].

Conclusions

The prevalence of wound sepsis at MRRH is high and most of the bacterial isolates were susceptible to 3rd generation cephalosporin

and quinolones but resistant to most penicillins. Severe anaemia, prolonged rupture of membranes, diabetes mellitus, multiple vaginal examinations (over four times), prolonged labour (over 18 hours), patients referred from peripheral health facilities, preoperative and postoperative antibiotic use, abnormal BMI and less than four times antenatal attendance were factors associated with development of post Cesarean wound sepsis.

What is already known on this topic?

1. Administration of pre-operative antibiotics within 30 to 60 minutes of skin incision reduces risk of postoperative infection by almost 70%.
2. Women giving birth by Cesarean section have a 5- to 20-fold greater risk of postpartum sepsis than women giving birth vaginally.

What this study adds

1. Prolonged rupture of membranes predisposes to wound infection.
2. The mothers who had more than four vaginal examinations in labour were more likely to develop wound sepsis.

Competing Interests

The authors declare no competing interests.

Authors Contributions

Joseph Isanga conceptualized the research idea, collected and analyzed data, drafted the manuscript and participated in critical revisions; Joseph Ngonzi conceptualized the research idea, analyzed data, drafted the manuscript and participated in critical revisions; Kayondo Musa participated in critical revisions; Julius Mugisha participated in critical revisions; Ronald Mayanja participated in data analysis and critical manuscript revisions; Leevan Tibaijuka participated in critical manuscript revisions and Emmanuel Byaruhanga participated in data analysis and critical manuscript revisions. All the authors have read and agreed to the final manuscript.

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