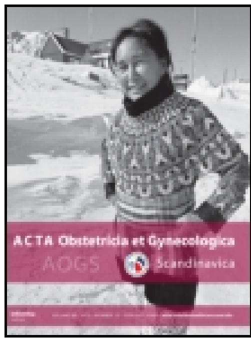

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Acta Obstetricia et Gynecologica Scandinavica

ISSN: 0001-6349 (Print) 1600-0412 (Online) Journal homepage: http://www.tandfonline.com/loi/iobs20

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To cite this article: Kenneth Björklund, Twaha Mutyaba, Evelyn Nabunya & Florence Mirembe (2005) Incidence of postcesarean infections in relation to HIV status in a setting with limited resources, Acta Obstetricia et Gynecologica Scandinavica, 84:10, 967-971

To link to this article: http://dx.doi.org/10.1080/j.0001-6349.2005.00875.x

Published online: 03 Aug 2009.

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Acta Obstetricia et Gynecologica Scandinavica

ORIGINAL ARTICLE

Incidence of postcesarean infections in relation to HIV status in a setting with limited resources

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Background. The aim of the present study was to assess the incidence of postcesarean infections in relation to HIV status in a setting where resources are limited, HIV infection is common, and antiretroviral treatment is not generally available.
Methods. The setting was a tertiary African obstetric unit with 27 000 deliveries annually. The study design was prospective and the sample consisted of 1600 of cesarean sections. All women requiring cesarean section were eligible for inclusion. HIV status was registered from the antenatal card only. For the analysis, the participants were divided into two categories: those with negative or unknown HIV status and those with positive HIV status. The main outcome measures are endometritis, wound infection, and mobilization parameters.
Results. A total of 1526 cases, of which 1492 were emergency cesarean sections, were included in the analysis. HIV status was negative or unknown in 1430 cases and positive in 96. In the HIV-negative/unknown group, the incidence of endometritis was 8.5% (121/1430), wound infection 5.0% (71/1430), and endometritis and/or wound infection 10.8% (154/1430). In the HIV-positive group, the corresponding incidences were 51.0% (49/96), 29.2% (28/96), and 65.5% (63/96), respectively. The indication for cesarean section was dystocia in 79% (134/170) of the women who developed endometritis.
Conclusions. The results indicate that women with untreated HIV infection are at very high risk of postcesarean infection in low-resourced settings.

Key words: cesarean section; endometritis; wound infection; HIV

Submitted 24 November, 2004
Accepted 1 April, 2005

Postpartum infection is the most frequent complication arising from cesarean delivery, with an incidence up to 20-fold that associated with vaginal delivery. Endometritis is the most common postcesarean infection, and wound infection is typically associated with endometritis. Major risk factors for postcesarean endometritis include primary cesarean section, young age, low socioeconomic status, frequent vaginal examinations, long duration of labor, chorioamnionitis, and immunodeficiency (1).

HIV infection and AIDS-related deaths have become a major cause of maternal mortality in many resource-poor settings. HIV infection also impacts on direct maternal mortality by an associated increase in pregnancy complications including puerperal sepsis (2). It is to be expected that women with untreated HIV infection are vulnerable to postoperative infection after cesarean section in such circumstances.

Many of the countries hardest hit by the HIV-AIDS pandemic are among the poorest in the world and cannot provide antiretroviral treatment to their citizens. In such resource-poor settings, delay is a key risk factor in obstetrics such as delay at home before recognition of the

problem, delay before the decision to seek help is made, delay in transport, and delay within health facilities. Cesarean section is therefore often not timely, and obstructed labor and infection aggravated by delay pose serious threats. The risks associated with delay may therefore converge with those of a high prevalence of untreated HIV infection.

The purpose of the present study was to assess the incidence of postoperative infections after cesarean section in women with and without known HIV infection in such an environment.

Subjects and methods

The trial was carried out at Mulago Hospital, Kampala, Uganda, a tertiary center with 27 000 deliveries a year and 300 cesarean sections a month. Any woman due for cesarean section, who gave her informed consent, was eligible for inclusion. There were no exclusion criteria. All doctors serving at the unit were invited to take part in the trial. The primary endpoint was the postoperative incidence of endometritis and wound infection.

The primary purpose was to analyze the endpoints in relation to surgical method. For this purpose, the study population was randomized to Misgav Ladach (3) or standard cesarean section, the latter defined as cesarean section as normally carried out at the unit, using a midline or a Pfannenstiel incision. The sample size required to detect a difference between the two groups was estimated at 800 cases in each arm, i.e. a total of 1600 cases, based on data from a previous trial in the region (4). The analysis of outcome by surgical method will be reported separately.

The second purpose was to analyze the primary endpoints in relation to HIV status, which is the topic of this article. To this end, information on HIV status was acquired from the antenatal card of women who had done a previous voluntary test. No woman was tested for HIV within the study, and the HIV serostatus was registered as either negative/unknown or positive in the trial. Since <100 known HIV-positive cases were included in the trial, the power is insufficient for an analysis of outcome by surgical method in this context. The description and analysis in this article are therefore based on HIV serostatus only.

The data collection was organized as follows. The surgeon registered baseline data and operative outcome in a data sheet that followed the patient to the ward, where two senior midwives ensured the registration of postoperative outcome, consulting a doctor as needed. A blood sample for hemoglobin was drawn immediately before the operation and on the third postoperative day. Drabkin's reagent and a colorimeter were used to assess the hemoglobin level by the cyanmethemoglobin method.

The trial commenced on 16 July 2001 and ended on 8 January 2003. During this period, approximately 5400 cesarean sections were carried out at the unit, of which 1600 were included in the study (30%). Thirty doctors took part in the study. During the course of the trial, 83 data forms were lost (5%), evenly distributed over the whole series. In another nine cases, a randomization slip had obviously been used twice, giving two data forms with the same serial number. The documentation available therefore comprises 1600 − 83 + 9 cases, i.e. 1526 cases. With no obvious ground for retrospective exclusions in this part of the study, all 1526 cases were included in the analysis.

General anesthesia, mostly ether, was used in 1496 of the operations, spinal in 26, both spinal and general anesthesia in three, and one case not stated. Booking status was registered for 1491 of the women, 956 as booked and 535 as unbooked, 1492 operations were registered as emergency cesarean sections and 15 as elective, 19 not stated. Oxytocin was given in 1470 of the cesarean sections. Misgav Ladach technique was used in 761 operations, standard cesarean section with midline incision in 696, and Pfannenstiel incision in 68 operations. In one case, the operative method was not registered.

Antibiotics were given as prophylaxis, treatment or both to 1495 of the 1526 women, starting before the cesarean section in 346 of cases and after the operation in 1149. Of the 31 women who received no antibiotics, nine were HIV positive. Benzyl penicillin G was used as standard prophylaxis. Expectant mothers with known positive HIV status were routinely provided one 200 mg tablet of Nevirapine at the antenatal clinic and instructed to ingest the tablet when labor starts to reduce the risk of mother to child transmission (5). Only two of the patients were on antiretroviral treatment.

Statistical analysis of continuous variables was carried out using Student's *t*-test and in one case estimation of relative risk. For categorical variables, Pearson's χ^2-test was used. The software used was the Statistical Package for the Social Services. Ethical approval for the study was obtained from the Mulago Hospital Research Committee, Kampala, Uganda, and the Ethics Committee of Uppsala University, Sweden. Each woman who participated in the study gave her informed consent.

Results

The HIV serostatus was negative or unknown in 1430 of the study participants and positive in 96. The mean age was 22.3 and 22.6 years, respectively, in these two groups (mean difference: −0.3 years, 99% CI −1.1 to 1.7), mean number of pregnancies 2.3 and 2.5, respectively (mean: −0.2, 99% CI −0.3 to 0.7), and mean parity 1.2 and 1.4, respectively (mean: −0.2, 99% CI −0.3 to 0.7).

Table I outlines the indications for cesarean section, where dystocia was the leading cause.

Table II gives details on operative outcome, with statistically significant differences in blood loss, number of blood transfusion, and Apgar score to the disadvantage of the HIV-positive group.

Table III summarizes that one in two of the HIV-positive women developed endometritis and two-thirds endometritis and/or wound infection, an incidence six times higher than that of the women with negative or unknown serostatus. Eight of the nine HIV-positive women who did not obtain any antibiotics developed endometritis, compared to five of the 22 with negative or unknown HIV serostatus. Overall, the indication for cesarean section was dystocia in 134 of the 170 cases that developed endometritis (79%).

Details of the infections were registered as follows: The diagnosis endometritis ($n = 170$) was set on average 2.6 days (range 1–4 days) after the

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Table I. Distribution of the indications for the cesarean section in the trial

	HIV serostatus			
	Negative/unknown, % (*n*)	Positive, % (*n*)	Chi-square	*P*-value
Dystocia*	53.0 (758)	53.1 (51)	0.001	0.982
Previous c/s	13.4 (192)	9.4 (9)	1.291	0.296
Fetal distress	9.8 (140)	10.4 (10)	0.040	0.842
Hypertensive disease	5.9 (85)	9.4 (9)	1.832	0.176
Breech	5.7 (81)	3.1 (3)	1.115	0.291
Haemorrhage†	4.6 (66)	4.2 (4)	0.041	0.839
Others‡	7.6 (108)	10.4 (10)	1.034	0.309
Total	1430	96		

*Seronegative/unknown: arm prolapse ($n = 19$), uterine rupture ($n = 13$). Seropositve: arm prolapse ($n = 1$)
†Seronegative/unknown: placental abruption ($n = 23$), placenta previa ($n = 22$). Seropositive: placenta previa ($n = 4$)
‡Seronegative/unknown: cord prolapse ($n = 15$)

operation with the following findings: tender uterus 31.2% (53/170), foul vaginal discharge 94.7% (161/170), and fever >38° on day 2 or later 83.5% (159/170). The diagnosis wound infection ($n = 99$) was set on average 3.6 days (range 2–6 days) after the operation with the following findings: discharge 78.8% (78/99), pus 91.9% (51/99), gapping 63.6% (63/99), wound rupture 4.0% (4/99), fever >38° day 2 or later 93.9% (93/99). Secondary suture was required in 74.7% (74/99) of cases.

The duration of hospital stay in relation to endometritis and wound infection with HIV status not taken into account was as follows: no endometritis or wound infection ($n = 1309$) 6.3 days (SD 1.6, range 4–16); endometritis but no wound infection ($n = 118$) 11.4 days (3.3, 6–39); wound infection but no endometritis ($n = 47$) 15.2 days (2.8, 9–21); endometritis and wound infection ($n = 52$) 15.9 days (3.0, 10–28). Table IV, finally, describes postoperative mobilization in relation to endometritis, wound infection, and HIV serostatus.

There were three maternal deaths. A 21-year-old woman, primigravida, unbooked, died on the second postoperative day from septicemia with paralytic ileus. A 19-year-old woman, gravida three, para one, unbooked, died immediately after the operation. She presented with an arm prolapse and a ruptured uterus, detected upon laparotomy and repaired. The cause of death was exsanguination and there was no blood in the blood bank. Another 19-year-old woman, primigravida, booked, died under resuscitation attempts in the recovery room. Autopsy showed the cause of death to be esophageal intubation. All three deceased had negative or unknown HIV status.

Discussion

Most previous studies on postcesarean infection rates in HIV-positive women stem from Europe and the United States. In those studies, about 80% of the women received antiretroviral treatment and 70% of the cesarean sections were elective. The overall reported incidence of endometritis was about 8% (range 0–17%) and that of wound infection about 7% (range 1–27%), with little differences compared to HIV-negative

Table II. Operative outcome

		HIV serostatus		
	n	Negative/unknown ($n = 1430$)*	Positive ($n = 96$)*	Difference†
Duration of c/s‡ (min)	1425	25.6 (8.7)	26.0 (7.1)	−0.4 (−2.0 to 2.8)
Preoperative Hb§ (g/dl)	1389	12.1 (1.5)	12.8 (1.7)	−0.6 (−1.1 to −0.2)
Postoperative Hb day 3§ (g/dl)	1378	11.0 (1.6)	11.1 (1.7)	−0.1 (−0.3 to 0.6)
Hb difference preoperative day 3§ (g/dl)	1370	1.1 (0.8)	1.7 (1.2)	−0.6 (−0.8 to −0.3)
Apgar score at 1 min	1407	8.2 (2.2)	7.3 (3.0)	0.9 (0.2–1.5)
Apgar score at 5 min	1368	9.2 (2.0)	8.3 (3.3)	0.9 (0.3–1.5)

*Values are expressed as mean (SD)
†Values are expressed as mean (99% CI)
‡Operating time including bilateral tubal ligation ($n = 104$) and repair ($n = 11$) or subtotal hysterectomy ($n = 2$) in the 13 cases of ruptured uterus
§Excluding the 37 cases where blood transfusion was given; n=29/1430 (2.0%) in the seronegative /unknown group and n=8/96 (8.3%) in the seropositive group (Chi-square 15.118, $P < 0.001$)

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Table III. Incidence of endometritis and wound infection in relation to HIV status in the study population during the postoperative recovery period

	HIV serostatus		
	Negative/unknown ($n = 1430$)*	Positive ($n = 96$)*	Relative risk (CI 99%) HIV positive
Endometritis	8.5 (121)	51.0 (49)	6.0 (4.2–7.8)
Wound infection	5.0 (71)	29.2 (28)	5.9 (3.4–8.3)
Endometritis and/or wound infection	10.8 (154)	65.6 (63)	6.1 (4.6–7.6)

*Values are expressed as % (n)

controls (6–15). In a study from Thailand, where all HIV-positive women received antiretroviral treatment and all cesarean sections were elective, an incidence of 3% of endometritis and 2% of wound infections was reported both in HIV-positive cases and HIV-negative controls (16). In a South African study with 85% emergency cesarean sections and no mention of antiretroviral treatment, the reported incidence of endometritis was 24% in HIV-positive women and 7% in HIV-negative controls, and that of wound infection 7 and 3%, respectively (17). In 2002, South Africa's Gross Domestic Product (GDP) per capita was estimated at 9401 USD per annum (18).

The present clinical trial was carried out by regular staff at a tertiary obstetric unit in a country with a total public (government and donor) allocation to health of less than 10 USD per capita per annum (19) and an estimated annual GDP per capita of 1208 USD (2002) (18). The results indicate that women with untreated HIV infection are at a very high risk of postcesarean infection in such low-resourced settings.

There were shortcomings in the present trial. First, only 30% of the cesarean sections were included. The main reason was that incoming new residents had to be trained in the Misgav Ladach technique before joining the study, and the process was slow. Second, 81 data forms were lost. The distribution of the losses was analyzed by dividing the 1600 serial numbers into groups of 200, i.e. No. 1–200, 201–400, etc., and checking the number of lost forms per batch of 200, which was 11, 6, 3, 9, 11, 13, 18, and 12, respectively. It was not possible to establish whether the losses were accidental and sporadic only, or if some had been intentional. Third, a tender uterus was reported in only 53 of 170 cases of endometritis. Inadequate design of the data form may have contributed, as there was a box for confirming tender uterus, but none for denoting absence of tenderness, and none for confirming that the uterus was examined for tenderness in the first place.

The expected HIV prevalence in the study population was retrospectively estimated at

Table IV. Mobilization and discharge by HIV status and presence or absence of endometritis and/or wound infection

	HIV serostatus		
	Negative/unknown*	Positive*	Difference†
No endometritis or wound infection			
	$n = 1276$	$n = 33$	
Out of bed (hours)	16.6 (5.3)	20.3 (4.5)	−3.7 (−1.3 to −6.1)
Touch toes (days)	1.5 (0.5)	1.8 (0.5)	−0.3 (−0.1 to −0.6)
Walk straight (days)	1.9 (0.9)	2.5 (0.8)	−0.6 (−0.2 to −1.0)
Pain eases (days)	3.8 (1.4)	5.0 (1.6)	−1.2 (−0.5 to −1.9)
Discharge (days)	6.3 (1.6)	7.7 (2.2)	−1.4 (−0.6 to −2.1)
Endometritis and/or wound infection			
	$n = 154$	$n = 63$	
Out of bed (hours)	20.8 (4.3)	22.8 (3.4)	−1.9 (−0.3 to −3.5)
Touch toes (days)	1.9 (0.4)	2.0 (0.3)	−0.1 (0.1 to −0.3)
Walk straight (days)	2.7 (0.6)	2.9 (0.5)	−0.2 (0.1 to −0.4)
Pain eases (days)	8.3 (3.0)	8.3 (1.9)	0.1 (1.1 to −1.1)
Discharge (days)	13.3 (4.0)	13.2 (3.1)	0.1 (1.5 to −1.4)

*Values are expressed as mean (SD)
†Values are expressed as mean (99% CI)

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8–9%, using surveillance data from the Uganda Ministry of Health AIDS Control Programme (20). The number of women with known HIV infection in the study was 96 of 1526 (6.3%). The group comprising women with negative or unknown HIV status ($n = 1430$) may thus be estimated to include 30–40 HIV-infected women, or <3%.

In summary, the aim of the present study was to assess the incidence of postcesarean endometritis and wound infection in relation to HIV status in a low-resourced setting where antiretroviral treatment is not generally available. The results indicate that HIV-infected women are at a very high risk of postcesarean infection in such settings.

Acknowledgments

The authors thank the residents, midwives, nurses, and the laboratory technician who took part in the study at Mulago Hospital. Financial support from the Swedish International Development Cooperation Agency (SIDA) is gratefully acknowledged.

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