



Sepsis: Primary indication for peripartum hysterectomies in a South African setting

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Background. Peripartum hysterectomies are lifesaving procedures but definitions vary. Indications are variable and dependant on resources and geographical factors.

Objectives. To evaluate the incidence, aetiology and complications associated with peripartum hysterectomies in a tertiary hospital in South Africa.

Methods. A retrospective audit at an academic referral centre over a 5-year period from February 2009 to March 2014 was performed. Procedures from a gestation of 24 weeks until 6 weeks postpartum were included.

Results. One hundred and sixty cases met inclusion criteria. Nine case records were unavailable. The incidence was 2.77 per 1 000 deliveries. Main indications were sepsis (60, 39.7%), atony (24, 15.9%), morbidly adherent placenta (21, 13.9%), tears (14, 9.3%), uterine rupture (8, 5.3%), placenta praevia (7, 4.6%) and unclassified bleeding (6, 4.0%). There were 6 maternal deaths. Five related to sepsis and one to hypovolaemic shock. One hundred and thirty-eight (91.4%) women required high or intensive care admission.

Conclusion. Sepsis is an important aetiology for peripartum hysterectomies, particularly in southern Africa. The high rate of sepsis may be due to HIV infection, low socioeconomic standards, late diagnosis, limited access to healthcare, sterility issues and differences in the definition and inclusion criteria used for a peripartum hysterectomy.

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A peripartum hysterectomy is a lifesaving procedure usually performed as an emergency that can be associated with significant morbidity and mortality.^[1] Despite many publications, the definition of a peripartum hysterectomy remains vague. Definitions include a hysterectomy performed within 24 hours of delivery,^[2-5] a hysterectomy performed within the same hospitalisation,^[6-10] a hysterectomy performed within 72 hours of delivery,^[11] a hysterectomy performed within 1 month of delivery^[12,13] to a hysterectomy performed within 6 weeks of delivery.^[14] Some even limit the definition to a hysterectomy performed for uncontrolled haemorrhage only^[4,15-22] and exclude cases of infection.^[12] The varying definitions make it difficult to compare incidences and aetiology. If a short time period after delivery is used, complications related to sepsis and delayed haemorrhage may be underestimated.

Peripartum hysterectomies complicate about 1 in 1 000 pregnancies.^[23] The incidence is lower in higher-resource settings. In a large review from the USA the incidence was 0.77 per 1 000 deliveries^[10] while African countries have reported higher incidences ranging from 4.34 to 9.5 per 1 000 deliveries.^[9,14,17,19] Lack of antenatal and peripartum care due to limited resources, a high burden of HIV infection and a delay in recognising complications may be reasons for the higher incidences.

In high-resource settings complications of placentation are the most common indication for hysterectomy.^[5-8,11,12,22,24,25] In middle-income countries the aetiology is variable, with studies from Turkey, India and Thailand showing similar indications to high-resource settings but with higher rates of uterine rupture.^[4,15,16,21,26-28] Sepsis has been reported as an indication in low-resource settings. In Africa the most common aetiologies include uterine rupture, atonic uteri and sepsis.^[14,19,29-31]

Three studies performed in tertiary care settings in South Africa (SA) have shown particularly high rates of sepsis. A study performed in Mthatha showed that uterine atony, puerperal sepsis

and secondary postpartum haemorrhage made up 57% of the indications. The morbidly adherent placenta was the least common indication.^[9] In a review of cases from Durban, uterine rupture and sepsis made up 56% of the indications,^[29] and a study from Pretoria reported that puerperal sepsis was the second most common indication after ruptured uteri and accounted for 33% of peripartum hysterectomies.^[31]

Observational data in our department at Tygerberg Hospital, a tertiary referral centre in Cape Town, suggested that sepsis was a common indication. This study was therefore designed to systematically evaluate the incidence, aetiology and complications associated with peripartum hysterectomy in the unit.

Methods

A retrospective audit was performed at Tygerberg Hospital, a state academic referral centre over a 5-year period from February 2009 to March 2014. The study was approved by the Stellenbosch University Health Sciences Ethics Committee (S13/08/155). Cases were identified in theatre record books and individual case records were reviewed. Data were extracted and transferred to an MS Excel spreadsheet. The inclusion criteria were all peripartum hysterectomies performed from a gestation of 24 weeks until 6 weeks postpartum. Information on patients' age, gravidity, parity, gestation, HIV status, CD4 count, antiretroviral (ARV) use, medical history, past obstetric history, antenatal care and complications, intrapartum course, mode of delivery, intrapartum complications, postpartum complications, neonatal outcome, indication for hysterectomy, type of hysterectomy, surgical complications, estimated blood loss, high-care admissions, blood products required, morbidity, mortality and length of hospital admission was collected. Statistica version 9 (StatSoft, USA) was used to analyse the data. Descriptive statistics were used to describe the data. Frequencies

(counts and percentages), measures of location (mean and median) and spread (standard deviations and percentiles) were used, depending on the distribution of the data.

Results

In the 5-year period 172 hysterectomies were identified. Two emergency theatre books were unobtainable. These contained information on peripartum hysterectomies that may have been performed from 25 October to 9 December 2011 and from 4 July to 15 August 2013. It is estimated that information on 0 to 12 cases may be missing. Twelve cases were excluded as the surgery was performed before 24 weeks. Three hysterectomies were performed for gestational trophoblastic disease, 1 was performed for an extrauterine pregnancy and 8 were performed for miscarriages. Six of the hysterectomies performed for a miscarriage were for septic retained products and 2 were for morbidly adherent placentas.

Of the 160 cases that met the inclusion criteria, 9 individual case records were unavailable. Two of these women died and 7 were discharged. One hundred and fifty-one cases were therefore included in the analysis. Ninety-six of these women delivered at Tygerberg Hospital and 55 delivered at a referral centre and were transferred because of complications. During this time period there were 34 558 births at Tygerberg Hospital, giving an overall rate for peripartum hysterectomies at our institution of 2.77 per 1 000 deliveries.

The youngest patient was 14 and the eldest 46 (mean age was 30 years). The majority were multigravid with a range of 1 - 7 pregnancies. The mean gestation at delivery was 36 weeks with a range from 24 to 42 weeks. One hundred and twenty-nine women (85.4%) had one or more antenatal visits, with 22 women (14.6%) presenting for the first time in labour. One hundred and forty women had singleton pregnancies, 10 patients had twin gestations and 1 patient had a triplet pregnancy. Of the parous women, 57 had had a previous caesarean section, with 28 (18.5%) having had one previous caesarean section and 29 (19.2%) having had two previous caesarean sections.

Fifty women (33.1%) were HIV-positive. Of these, 33 (66.0%) were on ARV treatment (ART) and 18 (36.0%) had a CD4 count <350 when they first presented for antenatal care. During the time period of this study women were initially only started on lifelong ART if their CD4 count was <350. In July 2013 our national guidelines regarding ART in pregnant women changed. Since then all HIV-positive pregnant women are started on lifelong ART at their first

Table 1. Antenatal complications (N=151)

| | n (%) |
|-----------------------------------|-----------|
| Hypertensive-related disorders | 49 (32.5) |
| Hypertension | 17 (11.3) |
| Pre-eclampsia | 19 (12.6) |
| Pre-eclampsia with HELLP syndrome | 13 (8.6) |
| Diabetes mellitus | 5 (3.3) |
| BMI >40 | 14 (9.3) |
| PROM | 6 (4.0) |
| APH | 15 (9.9) |
| Antenatal sepsis | 0 (0) |
| HIV | 50 (33.1) |

HELLP = haemolysis, elevated liver enzyme levels, and low platelet levels; PROM = premature rupture of membranes; APH = antepartum haemorrhage.

Table 2. Indications for induction of labour (N=32)

| | n (%) |
|------------------------------------|-----------|
| Hypertensive-related disorders | 17 (53.1) |
| Hypertension | 3 (9.4) |
| Pre-eclampsia | 11 (34.4) |
| Eclampsia | 3 (9.4) |
| Intra-uterine fetal demise | 5 (15.6) |
| Postdate pregnancy | 4 (12.5) |
| Prolonged rupture of membranes | 3 (9.4) |
| Previous abruptio placentae | 2 (6.3) |
| Previous intrauterine fetal demise | 1 (3.1) |

Table 3. Reasons for unsuccessful inductions (N=25)

| | n (%) |
|----------------------------------|--------|
| Fetal distress | 8 (32) |
| Not progressing to active labour | 7 (28) |
| Poor progress during labour | 4 (16) |
| Cephalopelvic disproportion | 3 (12) |
| Uterine rupture | 2 (8) |
| Extrauterine pregnancy | 1 (4) |

antenatal visit. Other antenatal complications are documented in Table 1.

One hundred and two patients attempted a vaginal delivery. Twenty-eight delivered vaginally (18.5%) with 1 requiring an assisted ventouse delivery. Seventy women (46.4%) went into spontaneous labour and 32 (21.2%) were induced. Indications for induction of labour are documented in Table 2. Only 7 patients had a successful induction that resulted in a normal vertex delivery. The reasons for unsuccessful induction are detailed in Table 3.

One hundred and twenty-three women had a caesarean section. Twenty-seven (22.0%) were elective and 96 (78.0%) were emergency procedures. The indications for caesarean section are documented in Table 4.

The main indication for a peripartum hysterectomy was uterine sepsis (60 cases, 39.7%). Fifty-two (86.7%) of these women were delivered by caesarean section; the indications included fetal distress in 16 cases (30.8%), poor progress in 13 cases (25.0%) and failed induction in 7 cases (13.5%). Fifteen of the patients (25.0%) who developed uterine sepsis needing a hysterectomy were induced. Of these, 3 (20.0%) received misoprostol, 4 (26.7%) received dinoprostone (Prepidil), 3 (20.0%) received a balloon catheter, 9 (60.0%) had an artificial rupture of the membranes and 8 (53.3%) received oxytocin. Eight patients (53.3%) needed more than one induction method. Thirty-five patients (58.3%) went into spontaneous labour and 4 patients (6.7%) were not in labour. None of these women was diabetic. Four were morbidly obese. Twenty-one (35.0%) were HIV-positive and all of these women had either a CD4 count <350 (52.0%) or were not on ART (48.0%). The shortest time interval from delivery to hysterectomy for sepsis was 3 days. The majority were performed 7 - 14 days post-delivery, with the longest time interval being 41 days.

Uterine atony was the second most common aetiology. Of the 24 (15.9%) peripartum hysterectomies performed for uterine atony,

Table 4. Indications for caesarean section (N=123)

| | n (%) |
|---|-----------|
| Emergency caesarean section | |
| Fetal distress | 31 (25.2) |
| Poor progress | 17 (13.8) |
| Two previous caesarean sections in labour | 9 (7.3) |
| Failed induction of labour | 7 (5.7) |
| Cephalopelvic disproportion | 5 (4.1) |
| Elective caesarean section | |
| Morbidly adherent placenta | 14 (11.4) |
| Placenta praevia | 5 (4.1) |
| Two or more previous caesarean sections | 4 (3.3) |
| Multiple pregnancy | 2 (1.6) |
| Breech presentation | 2 (1.6) |

6 patients (25.0%) were multigravidas, 4 (16.7%) had a multiple pregnancy, 2 (8.3%) had macrosomic fetuses (estimated fetal weight more than 4 kg) and 8 (33.3%) had had a previous caesarean section. Eight (33.3%) had a vertex vaginal delivery and 16 (66.7%) had a caesarean section, with 8 (33.3%) being elective because of previous caesarean section(s), multiple pregnancy, breech presentation and suspected fetal macrosomia. Eight were emergency caesarean sections. Eleven women (45.8%) went into spontaneous labour and 5 (20.8%) had an induction of labour. Oxytocin infusion with artificial rupture of the membranes was the induction method most commonly used. Four of the 5 patients who had inductions were administered more than one induction method.

Morbidly adherent placenta was the third most common indication. Of the 21 cases 7 (33.3%) were emergency hysterectomies as spontaneous labour occurred or a significant antepartum haemorrhage occurred before the planned delivery date. Fourteen cases were elective caesarean hysterectomies. Five patients had had one previous caesarean section, 12 had had two previous caesarean sections and one patient had had a previous uterine evacuation of retained products. Three patients had had previous normal vertex deliveries.

There were 14 cases (9.3%) of peripartum hysterectomies related to uncontrollable bleeding from tears. Thirteen were tears at emergency caesarean section that extended into the right or left uterine artery. In one of these cases the tear extended into the cervix and in another the tear extended into the cervix and vagina. There was one case of a vaginal tear during a vaginal delivery that extended to the cervix that required a hysterectomy to control the bleeding.

Uterine rupture occurred in 8 cases (5.3%). Half of these women had previously delivered by caesarean section. One woman needed a hysterectomy after blunt abdominal trauma. She had a scarred uterus from a previous caesarean section and was 30 weeks pregnant. Three women went into spontaneous labour and 4 had an induction of labour, of whom 3 received misoprostol and 1 received Prepidil and a balloon catheter.

Seven women (4.6%) who had a caesarean section for placenta praevia required a peripartum hysterectomy for placental bed bleeding that was not controllable with conservative methods. Six women (4.0%) had a peripartum hysterectomy due to unspecified haemorrhage. In these cases the cause of haemorrhage was not specified in the medical records.

One hundred and one total abdominal hysterectomies were performed and 50 cases were subtotal hysterectomies. In 3 of the subtotal hysterectomies the cervical stump was removed at a relook laparotomy. The main indication for performing a subtotal hysterectomy was haemodynamic instability and surgical difficulty because of distorted anatomy and/or adhesions.

There were 6 cases of maternal deaths. We were unable to obtain the case records for 2 of these cases but the cause of death on the death certificate was reported to be septic shock. Sepsis was therefore the cause of death in 5 cases and hypovolaemic shock in 1 case. Of the 3 cases whose deaths were related to sepsis, where the clinical records were available, only 1 was HIV-positive. She was a 26-year-old with a CD4 count of 17, not on ART, who was known to have chronic hepatitis B infection with liver failure and a history of perforated peptic ulcer disease. She had a preterm vaginal delivery, complicated by disseminated intravascular coagulation (DIC) and multiple postpartum haemorrhages requiring repeated laparotomies and transfusions. She developed severe puerperal sepsis and had a septic uterus at the time of hysterectomy. She died after she had received 70 units of packed red blood cells, 71 units of fresh frozen plasma, 7 units of platelets and 7 units of cryoprecipitate during her hospital admission. The second death was a 41-year-old multigravida who did not receive any antenatal care. She had a vaginal delivery at term and presented in septic shock 3 days postpartum. She had a cardiac arrest and was successfully resuscitated but sadly died later that day. Postmortem examination confirmed active pelvic floor sepsis and tonsillar herniation due to brain oedema. The third woman was a 33-year-old who was induced at 38 weeks for hypertension. She had prolonged rupture of membranes and a caesarean section was performed for fetal distress. One week postpartum she presented in septic shock. At the referring hospital she suffered a cardiac arrest and was successfully resuscitated. A laparotomy was performed and a ruptured sigmoid colon was repaired. A repeat laparotomy was required as she was unresponsive to therapy and a total abdominal hysterectomy was performed. She later died as a result of neutropenic septic shock that was unresponsive to treatment. The maternal death related to haemorrhage and hypovolaemic shock involved a 19-year-old primigravida who was induced for a post-date pregnancy and received misoprostol followed by a balloon catheter. The membranes were then artificially ruptured and oxytocin was given. A caesarean section was performed for poor progress. At caesarean section an atonic uterus was diagnosed. She received ergometrine, prostaglandin F_{2α} and oxytocin. Uterine compression sutures and uterine artery ligation were performed without success. The abdomen and pelvis were then packed with swabs and she was transferred to Tygerberg Hospital. She suffered a cardiac arrest during the surgery and was successfully resuscitated. Unfortunately DIC developed and after two further laparotomies she died.

Peripartum hysterectomies were associated with significant morbidity. A total of 138 women (91.4%) required either intensive care admission or a high-care admission. The majority of women who did not require intensive or high-care admission were elective caesarean hysterectomy cases.

Forty-three women (28.5%) required one or more repeat laparotomies with one requiring nine relook procedures. Most women (137, 90.7%) required blood transfusions. The average (median) amount of packed red blood cells was 6 units with a range of 1 to 70 units. Ninety-six women (63.6%) were given fresh frozen

plasma. The average amount of fresh frozen plasma required was 4 units, with a maximum of 71 units. Fifty-two women (34.4%) required platelets. On average one pool of platelets was required, with a maximum of 7 units being used. Twenty-six patients (17.2%) required cryoprecipitate.

Sixty-nine women (45.7%) required continuous positive airway pressure support and 53 (35.1%) were ventilated, with 6 (4.0%) needing a tracheostomy as a result of prolonged ventilation. Twenty-two women (14.6%) required inotropic support, 21 (13.9%) developed renal impairment, 3 (2.0%) developed a deep venous thromboembolism and 3 (2.0%) developed a cardiomyopathy, 2 secondary to sepsis and 1 being diagnosed as a peripartum cardiomyopathy. The mean admission time from peripartum hysterectomy to discharge or death was 10.2 days.

Discussion

Sepsis is an important aetiology for a peripartum hysterectomy, particularly in southern Africa. In this study, sepsis was the most common indication for a peripartum hysterectomy. This is the first study, according to our knowledge, to report this finding. The high rate of sepsis may be due to the high incidence of HIV infection in our community, low socio-economic standards, limited access to healthcare, late diagnosis of complications, sterility issues in the labour ward and theatre, and differences in the definition and inclusion criteria used for a peripartum hysterectomy. If the definition for peripartum hysterectomy had been hysterectomy at delivery or within 24 hours of delivery, or a hysterectomy for uncontrolled haemorrhage, we would have had no cases of sepsis and the incidence in this study would have been significantly lower. Defining a peripartum hysterectomy as a hysterectomy performed within 6 weeks of delivery, which is in line with the World Health Organization (WHO)'s definition of maternal mortality,^[32] would result in more standard reporting enabling one to compare studies with greater accuracy. Some may argue that even hysterectomies due to miscarriages and gestational trophoblast disease should be included in the definition as these are also related to pregnancy. Improving access to ART is important as all the women who were HIV-positive who needed a hysterectomy for the indication of sepsis had a CD4 count <350 or were not using ART. Implementing the WHO treatment programme Option B+, which entails starting a single daily dose fixed-combination regimen for all HIV-positive women irrespective of the CD4 count and the stage of disease,^[33] may decrease the rate of sepsis.

Uterine atony, the morbidly adherent placenta, uterine and cervical lacerations and uterine rupture were also identified as important aetiologies for peripartum hysterectomies. The morbidly adherent placental spectrum of disease and uterine rupture is known to occur more commonly with previous caesarean sections,^[34] so avoiding unnecessary caesarean sections is important in decreasing the incidence of peripartum hysterectomies. Delays in self-referral, doctor referral and identification of complications have been described as contributing factors to increased morbidity and mortality.^[35] This is especially important in the case of sepsis and haemorrhage, where early identification and treatment may prevent a hysterectomy.

This study did not demonstrate that diabetes is associated with an increased risk for a peripartum hysterectomy, despite our high rate of sepsis and diabetes which is different to published literature.^[36] Induction of labour, particularly with prostaglandins, was less of a risk factor than anticipated.

This study highlights the high morbidity and mortality associated with a peripartum hysterectomy. Morbidity and mortality after a peripartum hysterectomy are high and the majority of deaths were associated with sepsis. This is particularly challenging as the majority of septic hysterectomies occur in countries where access to high care and intensive care facilities is limited.

Strengths of this study include the size of the sample and the definition of a peripartum hysterectomy used, which includes all hysterectomies performed until 42 days postpartum and does not limit the inclusion to only hysterectomies for uncontrolled bleeding. Disadvantages of the study include that it was a retrospective review.

Studies assessing the aetiology of peripartum hysterectomies should use a definition that extends to 42 days after the delivery to avoid missing cases of sepsis and delayed haemorrhage, and hysterectomies performed for all obstetric indications should be included.

Further research should be aimed at assessing why the incidence of sepsis is so high in certain areas, particularly South Africa.

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