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Peripartum hysterectomy incidence, risk factors and clinical characteristics in Ireland

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Condensation: Peripartum hysterectomy incidence in Ireland has been consistently low at one case in every 3000 deliveries and adherence to guidelines is generally high.

Short version of the article title: Peripartum hysterectomy in Ireland.

Abstract

Background: The incidence of peripartum hysterectomy (PH) shows fifty-fold variation worldwide (0.2–10.5/1000 deliveries) and risk factors include advancing maternal age and parity, previous caesarean section (CS) and abnormal placentation.

Objectives: In this first national study of PH in Ireland, our objectives were threefold: to describe the national trend in PH incidence over 15 years since 1999; to assess risk of PH associated with morbidly adherent placenta (MAP), placenta praevia and postpartum haemorrhage (PPH) during 2005-2013; and to describe the causes, interventions and outcomes of PH cases during 2011-2013.

Study Design: For the 15-year time-trend analysis, PH cases and denominator data were extracted from Ireland's Hospital In-Patient Enquiry database. Multivariate Poisson regression analysis assessed risk of PH associated with MAP, placenta praevia and PPH. In collaboration with the 20 Irish maternity units we carried out a three-year national clinical audit of severe maternity morbidity. PH was a notifiable morbidity and the audit included detailed review of MOH cases.

Results: In 1999-2013 there were 298 PH cases, a rate of 0.32/1000 deliveries. During the period 2005-2013, the PH rate was 50 times higher in deliveries involving PPH, 100 times higher with placenta praevia and 1000 times higher with MAP. During the clinical audit (2011-2013) there were 65 PH cases, a rate of 0.33/1000 deliveries, increasing with advancing age and parity. The reporting of abnormal placentation, primarily the co-occurrence of placenta praevia and MAP, was linked with previous CS. Fifty-six of the 65 cases suffered MOH, most commonly associated with placenta praevia, MAP and uterine atony. Prophylactic and therapeutic uterotonic agents were appropriately used in the majority of cases.

Conclusions: The incidence of PH in Ireland has been consistently low over 15 years, averaging one case every 3000 deliveries. The recognised risk factors of MAP, placenta praevia and PPH were independently associated with PH, with MAP being by far the strongest predictor. The vast majority of PH cases in our clinical audit were associated with MOH. Some deficiencies were noted in antenatal care, in certain elements of treatment and clinical governance protocols but adherence to guidelines was generally high.

Key words: Peripartum hysterectomy; major obstetric haemorrhage; postpartum haemorrhage; caesarean section; morbidly adherent placenta; placenta accreta; placenta praevia.

Introduction

Peripartum hysterectomy (PH), the concept of which was proposed in the 1700s, is a rare occurrence in modern obstetrics. In 1869, the 'gravid uterus was for the first time amputated from a living woman' by Horatio Storer.[1] The first premeditated PH after which both the infant and mother survived was performed by Eduardo Porro, in 1876.[2]

Nowadays PH is generally performed as a lifesaving measure in cases of major obstetric haemorrhage (MOH) when more conservative efforts fail. The most recent United Kingdom and Ireland Confidential Enquiry into Maternal Deaths reported 17 direct deaths due to obstetric haemorrhage, making it the third leading cause of direct maternal death (0.49/100,000 maternities).[3] Six of these women underwent PH. The report recommended 'early recourse to hysterectomy……if simpler medical and surgical interventions prove ineffective'. Past triennial reports, along with national and international guidelines echo this principle, emphasising that recourse to hysterectomy should not be delayed 'until the woman is in extremis…'. [4,5,6,7]

Rates of PH reported worldwide show fifty-fold variation (0.2[8] – 10.5[9]/1000 deliveries). The UK Obstetric Surveillance System (UKOSS) study found its incidence to be 0.41/1000 births.[10] This is in keeping with other nationwide studies - Denmark 0.24/1000[11], Holland 0.33/1000[12] and Canada 0.35/1000[13] - but higher rates of 0.82/1000[14] and 0.85/1000[15] have been reported in the USA and Australia, respectively. Euro-Peristat reported rates of caesarean hysterectomy for postpartum haemorrhage (PPH) for 17 European countries in 2010 ranging from 0.0/1000 deliveries in Wales to 1.3/1000 in Estonia.[16] An international systematic review and the UKOSS study identified the following risk factors for PH: advancing maternal age and parity, previous caesarean section (CS) delivery and abnormal placentation.[10,17]

In Ireland, high rates of PH in a single maternity unit prompted the establishment of an Inquiry in 2003.[18] This led to the first reported national PH rate of 0.28/1000 births for the period 1999-2003. While most Irish PH studies have been conducted in single institutions,[19,20] a 40-year review of PH in the three Dublin maternity hospitals was recently performed.[21] It reported a decrease in its incidence, from 0.9 to 0.2/1000 deliveries. The indication for PH also changed, with cases increasingly being attributed to morbidly adherent placenta (MAP), a finding in keeping with large international reviews. [12,14,15,22,23]

In this first national study of PH in Ireland, our objectives were threefold: to describe the national trend in incidence of PH over the 15 years since 1999; to assess the contribution to risk of PH made

by MAP, placenta praevia and PPH during 2005-2013; and, to describe the clinical characteristics, causes, interventions and outcomes relating to PH cases during 2011-2013.

Materials and Methods

Since 1999 all public maternity units in Ireland have contributed data to the Hospital In-Patient Enquiry (HIPE) database, thereby providing data on approximately 98% of all deliveries nationally. The HIPE system records diagnoses and procedures according to the International Statistical Classification of Diseases and Related Health Problems (ICD) using the Ninth Revision, Clinical Modification (ICD-9-CM) for hospital discharges in 1999-2004 and the Tenth Revision, Australian Modification (ICD-10-AM) for discharges in 2005-2013.

We used delivery as the unit of analysis, defined as a hospital discharge following delivery of one or more liveborn or stillborn babies and indicated by the ICD-9-CM diagnosis code V27 or the ICD-10-AM diagnosis code Z37. PH was defined as a delivery discharge with a recorded procedure code for hysterectomy (ICD-9-CM: 68.3-68.7 and 68.9; ICD-10-AM: 3565300, 3565301, 3565304, 3565700, 3565800, 3566100, 3566400, 3566401, 3566700, 3566701, 3567000, 3567302, 3575000, 3575302, 3575600, 3575603, 9044800, 9044801 and 9044802).

For the 15-year time-trend analysis (1999-2013), the annual number of delivery discharges and PH cases associated with vaginal delivery and CS delivery were obtained via Health Atlas Ireland. The HIPE system's use of ICD-10-AM since 2005 allowed data to be obtained separately for elective and emergency CS deliveries for 2005-2013. The annual PH incidence rate was calculated per 1000 deliveries. Joinpoint regression analysis was used to assess the presence of linear trends in the PH rate and to find years when there was a change in such linear trends.[24]

To assess the contribution made to risk of PH by MAP, placenta praevia and PPH, we focused on the period 2005-2013 when ICD-10-AM coding allowed the diagnosis of MAP to be recorded in the HIPE database. MAP may be recorded based on clinical diagnosis or histopathological examination but the basis for the diagnosis is not known from the HIPE data. We extracted the number of delivery discharges and cases of PH by maternal age and mode of delivery and with and without PPH, placenta praevia and MAP. We calculated the crude rate of PH by these variables with exact Poisson 95% confidence intervals (CIs) and crude incidence rate ratios (IRRs) based on univariate Poisson regression. We then undertook a multivariate Poisson regression analysis to estimate the independent effect of the variables on risk of PH. Mode of delivery was not included in the multivariate analysis as there were too few cases of PH among vaginal deliveries and it was evident

that diagnosis of placenta praevia was almost deterministically linked with delivery by CS. As is common when examining the effect of multiple factors on the risk of rare events, there was overdispersion, i.e. the observed variation was greater than in a Poisson process, which rendered the Poisson regression inappropriate. To address this we undertook negative binomial regression which provided adjusted IRRs and their 95% CIs.

In collaboration with the 20 Irish maternity units we carried out a clinical audit of severe maternity morbidity for the three-year period 2011-2013, having adapted the methods of the Scottish Confidential Audit.[25] PH, defined as hysterectomy performed following delivery of a pregnancy or at any time during the puerperal period, was a reportable morbidity in the Irish audit and required the completion of a brief notification form which recorded indication for PH and core maternal and perinatal variables. For PH cases involving MOH (defined as blood loss of at least 2500ml, transfusion of five or more units of blood or documented treatment for coagulopathy[25]), a more detailed form was completed.

Crude PH rates and IRRs were calculated as described above. Denominator data were extracted from the HIPE database for the overall PH rate and the PH rate by maternal age and for deliveries with and without MAP. Denominator data extracted from the 2011-2013 annual reports of the Irish National Perinatal Reporting System (NPRS) allowed the calculation of crude PH rates by nationality, parity and gestation at delivery. One unit did not contribute to our audit in 2011 and 2012 thereby reducing coverage to 95.2% of all Irish deliveries during the three years. For the calculation of PH rates, we excluded 2011-2012 deliveries in this unit from the HIPE denominator data and weighted the denominator data from the NPRS using the multiple 0.952.

The HIPE data extracted for this study and the data collected by the clinical audit of severe maternity morbidity do not contain personal identifiers and were therefore exempt from institutional review board approval.

Results

In the 15-year period 1999-2013, there were 298 cases of PH among 927,495 deliveries, a rate of 0.32/1000 deliveries (95% CI=0.29-0.36/1000). There was no notable variation or time trend in the national PH rate (Figure 1). The overall incidence among vaginal deliveries was low at 0.07/1000 deliveries (95% CI=0.05-0.09/1000) and this rate decreased during the 15 years (annual rate change= -0.006/1000, 95% CI= -0.012 to -0.001/1000, p-value=0.044) so that the rate of PH fell from 0.13/1000 vaginal deliveries in the triennium 1999-2001 (95% CI=0.08-0.21/1000) to 0.01/1000 in 2011-2013 (95% CI=0.00-0.05/1000). The rate of PH among CS deliveries was far higher at 1.09/1000

(95% CI=0.96-1.24/1000), on average 16 times the incidence among vaginal deliveries (IRR=16.57, 95% CI=12.10-22.69, p-value<0.001). The rate of PH among CS deliveries was volatile from year to year with no clear linear trends. There were four deaths among the 298 women who underwent a PH, suggesting a case fatality rate of 1.3% (95% CI=0.4-3.4%).

During the nine-year period 2005-2013, there were 198 cases of PH among 609,599 deliveries, an incidence rate of 0.32/1000 deliveries (95% CI=0.28-0.37/1000), identical to the rate for the period 1999-2013. There was tenfold variation in the crude rate of PH when examined by maternal age and a twentyfold difference by mode of delivery (Table 1). Respectively, PH was required following 17.5% of deliveries involving MAP, 2% involving placenta praevia and 0.5% involving PPH. Thus, the rate of PH was approximately 50 times higher in deliveries involving PPH, 100 times higher with placenta praevia and 1000 times higher with MAP. Considering these risk factors and maternal age together there was a five, ten and 90 times increased risk of PH associated with PPH, placenta praevia and MAP, respectively.

There were 65 cases of PH reported from 196,514 deliveries in 2011-2013, a rate of 0.33/1000 deliveries (95% CI=0.26-0.42/1000). This rate increased with advancing age and even more so with increasing parity (Table 2). As found for the period 2005-2013, almost half of PH cases in 2011-2013 involved MAP. The rate of PH was approximately 17%, 1000 times higher in deliveries with MAP than in deliveries without MAP. Of the 31 cases of MAP-indicated PH, 61.3% were suspected antenatally. All but two PH cases involved CS delivery and three quarters had one or more previous CS deliveries. Antenatal ultrasound for placental location was performed for 90.9% (n=40/44) of the women with a history of CS.

The reporting of abnormal placentation, primarily the co-occurrence of placenta praevia and MAP, as a causal factor for PH was linked with the woman's previous history of CS (Table 3). Abnormal placentation was a reported cause of PH for 23.1% (3/13), 60.0% (9/15) and 89.7% (26/29) of women with no, one and two or more previous CS deliveries, respectively.

Fifty-six of the 65 women who underwent a PH (86.2%) had a MOH. The nine non-MOH cases of PH involved delivery by elective CS. MAP was the indication in six non-MOH cases; cervical cancer, uterine anomaly and uterine rupture in a case of chorioangiocarcinoma were reported for the other three cases.

Of the 56 MOH-related cases of PH, a single cause of haemorrhage was reported for 25 cases (44.6%) with multiple causes reported for the other 31 cases (55.4%). The most commonly reported were placenta praevia, MAP and uterine atony, as illustrated in the area-proportional Venn diagram in Figure 2.[26] Uterine rupture was not reported in these cases of PH.

The majority of the 56 women who underwent a PH associated with MOH had received a prophylactic uterotonic agent (n=51, 91.1%; not received in two cases, 3.6%, not known in three cases, 5.4%). Similarly approximately 90% of the women were administered therapeutic uterotonic agents (n=50, 89.3%), the majority (n=42, 75.0%) received more than two agents. Six women received none (10.7%).

The reported haemostatic surgical procedures undertaken for the 56 women who experienced MOH who ultimately required a PH is detailed in Table 4. For the nineteen women who received no surgical intervention prior to hysterectomy, the main indication for PH was abnormal placentation (n=14, 73.7%) with only one being for uterine atony. Four women in this subgroup received no uterotonic agents for treatment of MOH prior to PH - three cases of MAP and one case of cervical carcinoma who underwent a planned radical hysterectomy.

The mean estimated blood loss in the 56 cases of PH involving MOH was 5558ml (range=1300-13000ml). All of these women received a blood transfusion with, on average, ten units being transfused (range=1-24). Haemoglobin levels prior to the MOH event were reported for 54 of the 56 women and indicated that one in three (n=18, 33.3%) were anaemic (Hb<10.5g/dl). Cell salvage was performed for three women (5.4%). Thirty-nine women (69.6%) were given blood products to correct coagulopathy. In at least 90% of cases, obstetric and anaesthetic consultants were reported to have been present at the time of MOH (n = 51, 91.1% and n=52, 92.9% respectively). For almost half of the MOH cases (n=27, 48.2%), it was reported that there was a case review or discussion in subsequent risk management meetings.

Of the total of 65 women who underwent a PH whether associated with MOH or not, half (n=34, 52.3%) were admitted to an intensive care unit (ICU) and five (7.7%) suffered a pulmonary embolism. Of the 60 babies delivered to the 65 women, half (n=29, 48.3%) were admitted to a neonatal ICU. Two babies, born prematurely, died in the neonatal period.

Comment

This first national study of PH in Ireland shows that the incidence is low and has been consistently low for 15 years, with approximately one case in every 3000 deliveries. This is similar to the rate in other European countries[10,11,12] and in Canada[13] but it is less than half the PH rate observed in the USA and Australia.[14,15] The reasons behind this level of international variation warrants investigation.

The recognised risk factors of MAP, placenta praevia and PPH were independently associated with PH, with MAP being by far the strongest predictor. Consistent with this, the in-depth clinical review highlighted MAP and co-occurring placenta praevia as the most frequent causal factors for PH. These factors were particularly relevant for those women previously delivered by CS. In keeping with guidelines[7], the vast majority of women with previous CS had antenatal ultrasound for placental location. Almost all women with MAP-indicated PH had previously been delivered by CS. An adherent placenta was suspected in 60% of these. While it is recognised that the definitive diagnosis of MAP can only be made at surgery, the observation that 40% of cases were not suspected highlights the need for improvements in antenatal detection.

In keeping with previous publications, the vast majority of PH cases in our clinical study were associated with MOH. The MBRRACE-UK report recommends early recourse to hysterectomy in this setting.[3] Even so, national and international guidelines recommend that treatment with uterotonic agents is still considered first line for management of both atony and placenta praevia/MAP.[5,6] Contrary to this, one in ten women in our study received no uterotonic therapy for management of MOH and not all of the women were administered a prophylactic uterotonic agent. Some women may decline prophylactic medications as part of a pre-discussed birth plan. This represents an opportunity not only to maintain education of medical and midwifery staff of the value of prophylaxis and treatment with uterotonics but also to educate women themselves. Furthermore, one in three MOH-related cases had no surgical intervention prior to PH. However, this may be explained by the fact that the majority of this subgroup had abnormal placentation as the indication for PH.

PH is frequently performed in emergency situations on the background of substantial blood loss, contributing to significant perioperative morbidity for these women.[27] It should be noted that, although recommended, cell salvage is not readily available in all Irish maternity units. One third of our study group who experienced MOH were anaemic (<10.5g/dl) prior to the event. As highlighted in the recent guidelines, low antenatal haemoglobin should be optimised prior to delivery.[3,28] Continued education of both staff and women of the importance of considering iron supplementation and consideration of repeated testing of haemoglobin in the third trimester is a priority for many in antenatal care.

The high reported presence of consultants from both obstetric and anaesthetic specialities is to be commended. However, potential opportunities for training may have been missed as it was reported that only half of the cases were discussed in risk management meetings.

Several limitations of our study are acknowledged. The range of data in Ireland's national inpatient database is limited. In particular, body mass index is not recorded and parity has only recently been included, although these were included in our clinical review. The clinical review was carried out in voluntary collaboration from the country's maternity units which involved midwives and doctors collating data without protected time in a poorly-serviced information technology environment. Effects on data completeness and quality cannot be ruled out. However, data extracted from the HIPE databases corroborates our audit's findings in terms of case-ascertainment. Furthermore, associations of similar magnitude were observed from analysis of both data sources. Evaluation of PH was limited due to the focus of our clinical audit on MOH. Several aspects of women's care could therefore not be commented on such as future fertility desires, operative techniques and intra-operative complications.

In conclusion, PH is relatively rare in Ireland, affecting one woman in every 3000 deliveries. Despite this, the irreversible consequences remain for the affected woman and her family. Morbidly adherent placenta, in association with previous Caesarean delivery, was the strongest predictor of PH. The study confirms, in the Irish context, the established association between previous CS, MAP and PH[29,30] and highlights the need for improvements in antenatal detection and management of abnormal placentation. It will be important to monitor whether such improvements help to maintain Ireland's low PH rate or increase it as a result of more planned Caesarean hysterectomies.

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Table 1. Incidence and risk of peripartum hysterectomy in Ireland in 2005-2013 by maternal age, mode of delivery, morbidly adherent placenta, placenta praevia and postpartum haemorrhage

		PH cases	Deliveries	PH rate (95%CI)	cIRR (95%CI)	aIRR (95%CI)
	All	198	609599	0.32 (0.28-0.37)		
Maternal age	<30 years	22	231016	0.10 (0.06-0.14)	1.00 (ref.)	1.00 (ref.)
	30-34 years	66	212107	0.31 (0.24-0.40)	3.27 [1] (2.02-5.29)	1.32 (0.42-4.18)
	35-39 years	82	138214	0.59 (0.47-0.74)	6.23 [1] (3.89-9.97)	2.12 (0.68-6.65)
	≥40 years	28	28262	0.99 (0.66-1.43)	10.40 [1] (5.95-18.18)	2.90 (0.87-9.60)
Mode of delivery	Vaginal	24	448623	0.05 (0.03-0.08)	1.00 (ref.)	
	Caesarean section	174	160976	1.08 (0.93-1.25)	20.20 [1] (13.19-30.96)	
MAP	No	103	609058	0.17 (0.14-0.21)	1.00 (ref.)	1.00 (ref.)
	Yes	95	541	175.6 (142.1-214.7)	1038.4 [1] (785.7-1372.2)	89.2 [1] (34.8-229.2)
Placenta praevia	No	131	606484	0.22 (0.18-0.26)	1.00 (ref.)	1.00 (ref.)
	Yes	67	3115	21.5 (16.7-27.3)	99.6 [1] (74.2-133.7)	10.6 [1] (4.5-25.1)
PPH	No	65	584556	0.11 (0.09-0.14)	1.00 (ref.)	1.00 (ref.)
	Yes	133	25043	5.31 (4.45-6.29)	47.8 [1] (35.5-64.3)	5.04 [1] (2.12-12.00)

PH, peripartum hysterectomy; PH rate per 1000 deliveries; CI, confidence interval; cIRR, crude incidence rate ratio; aIRR, adjusted incidence rate ratio from multivariable analysis including all other variables in the table except mode of delivery which was not included because there were too few cases of PH among vaginal deliveries and diagnosis of placenta praevia was almost deterministically linked with delivery by CS; MAP, morbidly adherent placenta; PPH, postpartum haemorrhage; [1] $P < .001$

Table 2: Characteristics and incidence of peripartum hysterectomy in Ireland in 2011-2013

Characteristic	Category	n (%)	PH rate (95%CI)	cIRR (95%CI)
All		65 (100.0)	0.33 (0.26-0.42)	
Age	<30 years	8 (12.3)	0.12 (0.05-0.24)	1.00 ref.)
	30-34 years	23 (35.3)	0.32 (0.20-0.48)	2.68 [3] (1.20-5.98)
	35-39 years	24 (37.0)	0.50 (0.32-0.74)	4.16 [1] (1.87-9.27)
	≥40 years	10 (15.4)	0.96 (0.46-1.77)	8.00 [1] (3.16-20.27)
Irish	Yes	40 (69)	0.26 (0.19-0.35)	1.00 (ref.)
	No	18 (31)	0.38 (0.22-0.60)	1.45 (0.83-2.53)
Parity	0	5 (7.7)	0.06 (0.02-0.15)	1.00 (ref.)
	1	18 (27.7)	0.26 (0.15-0.41)	4.07 [2] (1.51-10.97)
	2	19 (29.2)	0.55 (0.33-0.86)	8.64 [1] (3.22-23.13)
	≥3	23 (35.4)	1.26 (0.80-1.88)	19.80 [1] (7.53-52.07)
Previous CS	No	13 (22.8)		
	Yes, one	15 (26.3)		
	Yes, two or more	29 (50.9)		
BMI (kg/m^2)	Lean (<25)	17 (34.7)		
	Overweight (25<30)	15 (30.6)		
	Obese (≥30)	17 (34.7)		
Pre-term	No (≥37 weeks)	34 (53.1)	0.18 (0.12-0.25)	1.00 (ref.)
	Yes (<37 weeks)	30 (46.9)	2.34 (1.58-3.34)	13.26 [1] (8.12-21.66)
Delivery mode	Elective LUSCS	29 (44.6)		
	Emergency LUSCS not in labour	21 (32.3)		
	Emergency LUSCS in labour	11 (16.9)		
	Classical CS	2 (3.1)		
	Other	2 (3.1)		
MAP	No	34 (52.3)	0.17 (0.12-0.24)	1.00 (ref.)
	Yes	31 (47.7)	173.2 (117.7-245.8)	1000.1 [1] (614.7-1627.1)
Birthweight	<2500g	14 (24.1)		
	2500-3999g	40 (68.9)		
	≥4000g	4 (6.9)		

PH, peripartum hysterectomy; % adjusted for missing data; PH rate per 1000 deliveries; CI, confidence interval; cIRR, crude incidence rate ratio; BMI, body mass index; CS, caesarean section; LUSCS, lower uterine segment caesarean section; MAP, morbidly adherent placenta; Other delivery mode includes one non-rotational forceps and one case of chorioangiocarcinoma; [1] P < .001; [2] P < .01; [3] P < .05.

Table 3: Causal factors in cases of peripartum hysterectomy in 2011-2013 by number of previous caesarean section deliveries

Previous CS	Placenta praevia only	MAP only	Placenta praevia & MAP	Other causes	Total
No	2	0	1	10	**13 (22.8%)**
Yes, one	1	2	6	6	**15 (26.3%)**
Yes, two or more	7	6	13	3	**29 (50.9%)**
Total	10	8	20	19	**57**

CS, caesarean section; MAP, morbidly adherent placenta; Other causes were uterine atony (n=9) and bleeding from uterine incision (n=5) and cervical laceration, endometritis, pseudoaneurysm, cervical cancer and cervical pregnancy each caused one case; Previous history of CS was not reported for eight cases.

Table 4: Haemostatic surgical procedures in cases of peripartum hysterectomy involving major obstetric haemorrhage in 2011-2013

Procedure	**n (%)**
None	19 (33.4)
Intrauterine balloon tamponade	18 (32.7)
Intra-myometrial carboprost	8 (14.5)
Manual removal of placenta/retained tissue	7 (12.7)
Haemostatic brace uterine suturing	6 (10.9)
Bilateral ligation of uterine arteries	6 (10.9)
Re-suturing of uterine incision/suturing of lateral extension	5 (9.1)
Uterine artery embolization (interventional radiology)	3 (5.5)
Bilateral ligation of iliac arteries	2 (3.6)
Repair of vaginal/cervical lacerations	2 (3.6)
Other	5 (9.1)
Total	56 (100.0)

Other includes laparotomy, suturing of bladder and haemostatic suture to placental bed

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