Risk Factors Associated with Postpartum Hemorrhage in Western North Carolina

Stephanie T. Romero, MD, Shelley L. Galvin, MA, Maggie Harper, MD
Mountain Area Health Education Center, Department of Obstetrics and Gynecology Asheville, North Carolina

Objective: The rate of post partum hemorrhage (PPH) is increasing in the US, Canada, Australia, and Europe. The etiologies of this increase have not been well-defined. Our objective was to use primary data sources to estimate the risk of PPH associated with patient variables and practice patterns.
Study Design: We examined two years of deliveries (2008-2009) of singleton, live births at a regional referral center utilizing a case-control design to assess differences in patient variables and practice patterns. We matched controls to cases, 2:1, by delivery route. We used Student *t* test, X^2, Fisher exact test, and multivariate logistic regression to examine the relative contribution of risk factors to outcomes while controlling for known risk factors for PPH in order to elucidate any new risk factors apparent in our population.
Results: We analyzed 269 cases and 538 controls; 75.1% of deliveries were vaginal and 24.9% were cesarean. Significant predictors included Hispanic ethnicity, BMI > 40, pre-eclampsia, post-date pregnancies, shoulder dystocia and manual removal of placenta.
Conclusions: The results of this study confirm suspicions of an association between PPH and obesity (especially BMI $\geq$ 40). Improved knowledge about the risk factors for PPH can inform inter-conception counseling and PPH preventive measures at delivery.

Keywords: Postpartum hemorrhage; obesity; risk factors

Introduction

Acute postpartum hemorrhage (PPH) is a major cause of maternal mortality and morbidity worldwide, and of the ½ million women who have a pregnancy related death from a preventable cause, an estimated 25% are due to PPH.[1] Etiologies of PPH include uterine atony, retained placental tissue, abnormal placentation, genital tract trauma, and coagulation abnormalities. Of these, the most common is uterine atony. The rate of PPH is reported to be increasing in the US, Canada, Australia, and Europe.[2-4] The etiologies of this increase have not been well-defined. The recommendations from the International Postpartum Hemorrhage Collaborative Group include a call for more research into the potential risk factors for PPH, which they identified as "increased duration of labor, obesity, and changes in second and third stage management practice."[3] Our objective was to use primary data sources to estimate the risk of PPH associated with patient variables and practice patterns.

Methods

We examined deliveries occurring between January 1, 2008 and December 31, 2009 at a regional referral center serving western North Carolina. We utilized a case-control design to assess differences in patient variables and practice patterns for the 24-month period. Potential cases of PPH were identified using ICD9 codes 666.10-666.14, and charts were reviewed individually to confirm whether or not they met the inclusion criteria. Deliveries, matched for route of delivery,

immediately preceding and following each case delivery were chosen as controls, and those charts reviewed to ensure that they did not meet criteria as a case themselves. Multifetal pregnancies were excluded. The inclusion criteria were:

1. Live births;
2. Hemorrhage within 24 hrs of delivery; and
3. Estimated blood loss (EBL) $\geq$500mL for vaginal or $\geq$1000mL for cesarean delivery.

Any patient identified by ICD-9 code as a case who did not meet inclusion criteria was removed from the analysis. Any patient chosen as a control who was found to meet criteria for postpartum hemorrhage was classified and analyzed as a case, and an alternate control was chosen to replace it. In addition, two controls matched to the newly designated case were identified.

If discrepancies in EBL were noted, the physician's birth note became the study criterion. Qualitative descriptions of blood loss were reviewed clinically to determine if total EBL during the 24-hour period exceeded cutoffs when indicated.

Demographic variables, obstetric characteristics and interventions were abstracted using a standard form. Frequency distributions of variables were compared between cases and controls using Student *t* test, X^2, and Fisher exact test where appropriate. Multivariate logistic regression was used to examine the relative contribution of risk factors to outcome. We examined practice patterns and patient characteristics separately using variables identified as significantly different in univariate analyses. The final model combined significant predictors from the initial models and ultimately retained only significant predictors of PPH.

We controlled for known risk factors for PPH including prolonged 2nd stage of labor (nulliparas with anesthesia >180 minutes, without >120 minutes; multiparas with anesthesia > 120 minutes, without > 60 minutes), macrosomia ($\geq$4000 gm), chorioamnionitis, and diabetes (as diagnosed or indicated by the attending physician) in order to elucidate any new risk factors apparent in our population. Analyses were conducted using SPSS 18.0.1.[5]

Results

After review of the charts, a total of 269 cases and 538 controls were included in the analyses (see Figure 1). Routes of delivery and total estimated blood loss are shown in Table 1. Overall 75.1% of deliveries were vaginal and 24.9% were cesarean.

Univariate analyses of participant characteristics indicated that cases were more likely to be minorities and to have larger body mass indices (BMI) at time of delivery (see Table 2). Cases were also more likely to be nulliparous, to have medical complications of any type (especialy pre-eclampsia or chorioamnionitis), and to receive magnesium sulfate in labor (see Table 3). Birth outcomes comparisons indicated cases were more likely to be post-term deliveries (>40 weeks). Twice as many infants with macrosomia were born to cases, and the incidence of shoulder dystocia was four times higher among cases than controls (see Table 4). Practice patterns were significantly different as cases underwent manual removal of the placenta and required pharmacotherapy and/or procedures to control bleeding more frequently than controls (see Table 4). The rate of induction of labor was not significantly different; the use of any oxytocin during labor, however, was greater in cases.

Figure 1. Flow Chart for PPH Cases and Controls

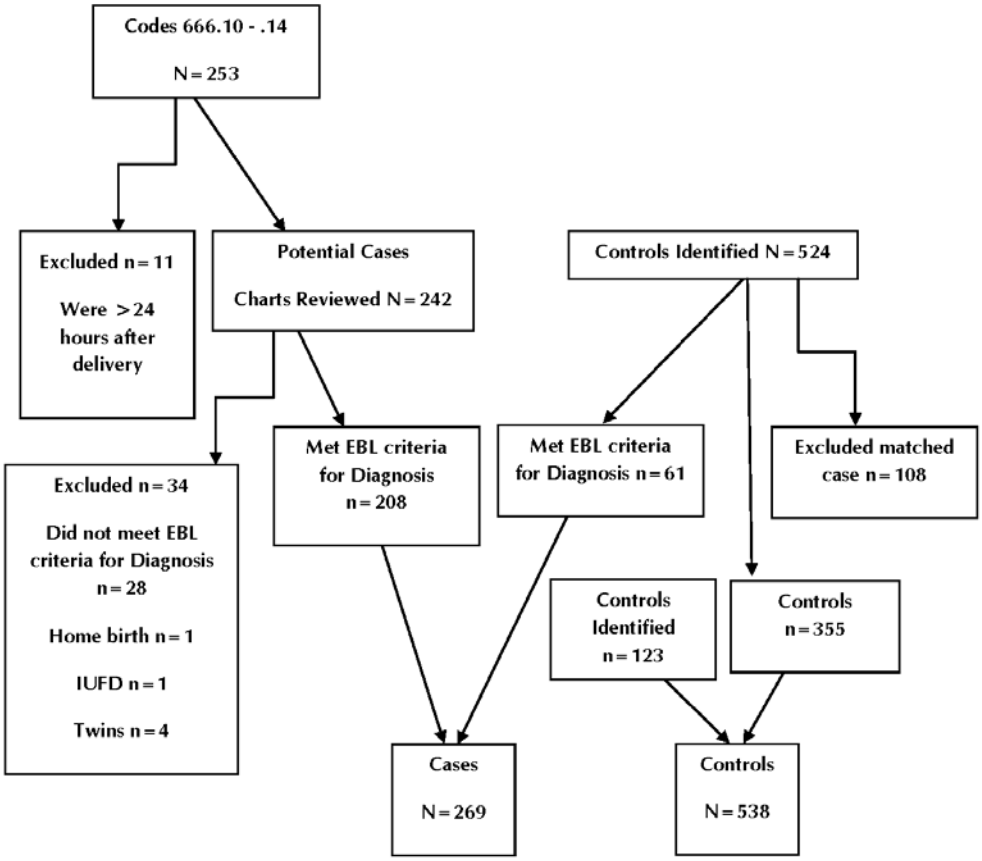

Table 1. Matched Routes of Deliveries and Estimated Blood Loss

	Cases N = 269	Controls N = 538
Delivery: Vaginal Delivery	202 (75.1)	404 (75.1)
Spontaneous vaginal delivery	188 (69.9)	376 (69.9)
Vacuum extraction	11 (4.1)	22 (4.1)
Forceps	1 (0.4)	2 (0.4)
Vaginal birth after cesarean delivery (VBAC)	2 (0.7)	4 (0.7)
Delivery: Cesarean Delivery	67 (24.9)	134 (24.9)
Primary cesarean (PC)	46 (17.1)	92 (17.1)
Scheduled	4 (8.7 of PC)	8 (8.7 of PC)
Repeat cesarean (RC)	21 (7.8)	42 (7.8)
Failed VBAC	1 (4.8 of RC)	2 (4.8 of RC)
Estimated Blood Loss (EBL): Vaginal Delivery	600 ml (500 – 3000 ml)	300 ml (100 – 450 ml)
Estimated Blood Loss (EBL): Cesarean Delivery	1225 (1000 – 6500 ml)	700 ml (400 – 950 ml)

Note. EBL presented as median (minimum-maximum)

Table 2. Patient Socio-demographic Characteristics

		Cases N = 269	Controls N = 538	P
Age	≤ 19 years	29 (10.8)	56 (10.4)	0.472
	20 – 34 years	213 (79.2)	412 (76.6)	
	≥ 35 years	27 (10)	70 (13)	
Race	White	187 (70.3)	428 (80.9)	0.002
	Black	22 (8.3)	40 (7.6)	
	Hispanic	46 (17.3)	46 (8.7)	
	Other Minority	11 (4.1)	15 (2.8)	
	Unknown	3 (1.1)	9 (1.7)	
Relationship status				0.157
	Partnered	144 (55.2)	312 (60.5)	
	Single	117 (44.8)	204 (39.5)	
	Unknown	8 (3)	22 (4)	
Body Mass Index (BMI) @ delivery		31.4 (19.7-52.4)	29.9 (18.8-73.7)	0.005†
BMI category	≥ 40	28 (10.6)	47 (8.8)	0.012
	35-39.99	41 (15.6)	64 (12)	
	30-34.99	94 (35.7)	154 (28.8)	
	< 30	100 (38)	269 (50.4)	
	Unknown	6 (2.2)	4 (0.7)	

Note. *Frequency (Percent); Chi square test
†Median (minimum-maximum); Mann-Whitney U test

Table 3. Antepartum Characteristics

		Cases N = 269	Controls N = 538	P
Previous deliveries	Nulliparous	150 (55.8)	248 (46.1)	0.010
	Multiparous	119 (44.2)	290 (53.9)	
Prenatal Medications				
Selective serotonin reuptake inhibitors (SSRI)		13 (4.8)	23 (4.3)	0.718
Anticoagulants		2 (0.7)	1 (0.2)	0.259*
Tocolytics	None	254 (94.1)	525 (97.2)	0.033
	Magnesium sulfate	14 (5.2)	11 (2)	
	Nifedipine	1 (0.4)	0	
	Turbutaline	1 (0.4)	4 (0.7)	
Co-morbid diagnoses				
Diabetes (Gestational or pre-gestational)		27 (10)	34 (6.3)	0.060
Pre-eclampsia		33 (12.3)	33 (6.1)	0.003
Anemia (< Hb10.5) ≤ 23 weeks gestation		29 (10.8)	37 (6.9)	0.056
Polyhydramnios		2 (0.7)	5 (0.9)	1.000*
Coagulation disorder		3 (1.1%)	4(0.7)	0.692*
History postpartum hemorrhage		1 (0.4)	2 (0.4)	1.000*
Placental abnormality		12 (4.5)	11 (2)	0.052
Chorioamnionitis		31 (11.5)	17 (3.2)	0.0001
Ehlers Danlos.		1 (0.4)	0	0.157*
Any of the above diagnoses		115 (42.8)	122 (22.7)	0.0001

Note. Chi square analysis unless otherwise indicated. *Fisher's Exact Test

Table 4. Practice Patterns and Delivery Outcomes

		Cases N = 269	Controls N = 538	P
Gestational age @ delivery				0.021
	Term: 37 – 40 weeks	159 (59.1)	359 (66.7)	
	Postterm: ≥ 40 weeks & 1 day	83 (30.9)	122 (22.7)	
	Preterm: 34 – 36weeks & 6 days	18 (6.7)	48(8.9)	
	Very preterm: ≤ 33 weeks & 6 days	9 (3.3)	9 (1.7)	
Birth weight	≥ 4000 grams	34 (12.8)	34 (6.3)	0.002
	< 4000 grams	232 (87.2)	504 (93.7)	
	Unknown	3 (1.1)	0	
Anesthesia: Vaginal delivery	None	36 (17.8)	67 (16.6)	0.586
(n = 606)	Local	15 (7.4)	26 (6.4)	
	Epidural	150 (74.3)	304 (75.2)	
	Spinal or CSE	1 (0.5)	7 (1.7)	
Anesthesia: Cesarean delivery	Epidural	33 (49.3)	67 (50)	0.085
(n = 201)	Spinal	28 (41.8)	64 (47.8)	
	CSE	2 (3)	0	
	General	4 (6)	3 (2.2)	
Oxytocin use in labor	None	98 (36.4)	238 (44.2)	
	Any	171 (69.8)	300 (61)	0.019
	Induction of labor	121 (45)	212 (39.4)	0.129
Prolonged second stage of labor (n = 581)		20 (10.8)	37 (9.3)	0.580
Shoulder dystocia		18 (6.7)	8 (1.5)	0.0001
Severe Lacerations (3rd or 4th degree)		9 (4.5)	11 (2.7)	0.4
Placental removal: Manual		79 (29.5)	115 (21.4)	0.011
Uterotonics (methylergonovine, prostaglandin, and/or misoprostol)		159 (59.1)	6 (1.1)	0.0001
Postpartum oxytocin		169 (72.8)	9 (1.7)	0.0001
Curettage		12(4.5)	1 (0.2)	0.001*
Hysterectomy		4 (1.5)	0	0.012*
Transfusion		31 (11.5)	1 (0.2)	0.0001

Note. Chi square analysis unless otherwise indicated.
*Fisher's Exact Test

Multivariate logistic regression models are shown in Table 5 and 6 for practice patterns and patient characterizes, respectively. Among the three significant practice patterns examined, manual removal of the placenta was most strongly associated with PPH. With regard to patient characteristics, Hispanic ethnicity, nulliparity, BMI ≥ 40, diagnosis of pre-eclampsia, delivery post-term, and shoulder dystocia increased the odds of PPH. The final model included all predictors except oxytocin (p = 0.325) or tocolytics (p = 186) in labor (see Table 7).

Table 5. Practice Patterns

	Reference	OR	95% CI	P
Tocolytics in labor	None	3.840	1.438-10.254	0.007
Oxytocin in labor	None	1.514	1.018-2.251	0.041
Manual removal of placenta	Spontaneous	6.279	2.789-14.135	0.001

Note. Nagelkerke $R^2 = 0.129$

Table 6. Patient Characteristics

	Reference	OR	95% CI	P
Multiparity	Nulliparity	0.496	0.331-0.744	0.001
Race/Ethnicity	White			
Other		1.930	0.535-6.958	0.315
Black		1.225	0.598-2.507	0.579
Hispanic		2.329	1.287-4.213	0.005
BMI	< 30			
> 40		2.158	1.102-4.227	0.025
35-39.99		1.533	0.843-2.790	0.162
30-34.99		1.294	0.820-2.042	0.267
Pre-eclampsia	None	2.859	1.405-5.818	0.004
Gestational age	37-40 weeks			
> 40 weeks		1.732	1.115-2.689	0.014
< 37 weeks		0.919	0.443-1.909	0.821
Shoulder dystocia	None	3.340	1.272-8.767	0.014

Note. Nagelkerke $R^2 = 0.174$

Table 7. Final Model

	Reference	OR	95% CI	P
Multiparity	Nulliparity	0.534	0.355-0.801	0.002
Race/Ethnicity	White			
Other		1.902	0.534-6.778	0.321
Black		1.365	0.664-2.808	0.397
Hispanic		2.481	1.370-4.492	0.003
BMI	< 30			
≥40		2.006	1.011-3.979	0.046
35-39.99		1.363	0.743-2.500	0.318
30-34.99		1.255	0.791-1.991	0.335
Pre-eclampsia	None	3.275	1.593-6.735	.001
Gestational age	37-40 weeks			
> 40 weeks		1.791	1.146-2.800	0.011
< 37 weeks		1.035	0.495-2.164	0.927
Manual Placental removal	Spontaneous	6.202	2.661-14.453	.0001
Shoulder dystocia	None	3.504	1.331-9.226	.011

Note. Nagelkerke $R^2 = 0.208$

Discussion

The results of this study confirm the suspicions of Callaghan et al, in that we found an association between PPH and obesity (especially BMI ≥ 40).[3] The prevalence of obesity in the United States and world-wide is increasing.[6] Other investigators have tried to link obesity to PPH. In one study, women with a BMI $>$ 30 had decreased risk of PPH.[7] Another study of over 3000 women did not find an association between obesity and PPH, although other causes of maternal morbidity and mortality were found to be associated with obesity.[8] In contrast, a retrospective cohort study of over 11,000 nulliparous New Zealanders demonstrated obese women had an approximate two-fold risk of PPH regardless of mode of delivery.[9] And another cohort study of over 1 million Swedish women found a significant correlation between maternal BMI and rates of PPH, particularly atonic PPH.[10]

Duration of labor is another one of the potential risk factors described by the International Postpartum Hemorrhage Collaborative Group, and we attempted to discern that, but the nature of the study made accurate evaluation of the first stage impossible due to the inconsistencies in charting the time of initiation of labor. Induction of labor, which is associated with an increased length of time in labor, was not a significant risk factor for PPH in our study ($p = 0.129$). In contrast, any use of oxytocin, which combines both induction and augmentation of labor, was associated with a significant increase in PPH.

Improved knowledge about the risk factors for PPH can help providers in two ways. First, it is another tool in the evaluation and education of women who are not pregnant, and provides an opportunity to practice preventive medicine. Second, women who present to the hospital for delivery can be evaluated and if found to be at high risk for PPH, preventive measures can be instituted, such as the administration of prophylactic uterotonics. The effectiveness of such measures should be investigated in future studies.

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Disclosure: None of the authors have a conflict of interest.
Financial Support: This study was underwritten by the MAHEC Department of Obstetrics and Gynecology

Paper presented at the NC OBGYN Society Meeting, Asheville, NC; April, 2011
Winner of the North Carolina Obstetrical and Gynecological Society Resident Research Award

Winner of the 2011 MAHEC Resident Research Day Audience Award

Reprints and Correspondence: Shelley L. Galvin, MA; MAHEC Department of Obstetrics and Gynecology, 119 Hendersonville Road, Asheville, NC 28803
Business 828.771.5501 Email: Shelley.Galvin@mahec.net