SUPPLEMENTAL MATERIAL

Risk Factors for Pregnancy-Associated Stroke in Women with Preeclampsia: a Case-Control Study

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Supplemental Table I. Pregnancy-specific stroke ICD-9 code validation

Background: Pregnancy-specific stroke ICD-9 codes have been used in epidemiological studies to identify pregnancy-associated strokes (PAS),[1-4] but may have poor positive predictive value (PPV).[5] We previously validated the sensitivity of these codes at 92%,[6] based on an internal stroke registry. However, this registry includes only cases adjudicated as strokes by a panel of vascular neurologists, and is not based on administrative data.

Methods: We queried the electronic medical record system at Columbia University Medical Center for ICD-9 codes 671.5, 674.01, 674.02, 674.03, and 674.04 for any diagnosis from January 1, 2010 through December 31, 2015. IRB approval was obtained to review the individual medical records of the patients identified. PAS was defined as any confirmed cerebrovascular event, including TIA, ischemic stroke, SAH, ICH, cerebral venous thrombosis, or clinically and radiologically confirmed reversible cerebral vasoconstriction syndrome (with or without hemorrhage or infarct).

Results: A total of 56 individual patients were identified with codes 674.0x. There were no patients with the code 671.5. Of the 56 identified patients, 45 (80.4%) had confirmed PAS. The clinical diagnoses among the 11 false positives included: brain tumor (1), chronic hypertension (1), unruptured aneurysm (2), asymptomatic moyamoya disease (1), delivery admissions for women with prior non-pregnancy related ischemic or hemorrhagic stroke (4), complicated migraine(1), and remote gunshot wound to the head (1).

Conclusions: In our sample at a tertiary care center, pregnancy-specific stroke codes had a PPV of 80.4%.

Case#	ICD-9 code (code position)	PAS (yes/no)	Timing	Clinical diagnosis
1	674.04 (5)	yes	Postpartum	Venous sinus thrombosis with ICH
2	674.04 (1)	yes	Postpartum	cardioembolic stroke
3	674.04 (1)	yes	Postpartum	RCVS with SAH
4	674.03 (1)	yes	Antepartum	cryptogenic stroke
5	674.03 (1)	yes	Antepartum	cerebellar ICH
6	674.04 (1)	yes	Postpartum	RCVS with SAH/ICH
7	674.04 (5)	yes	Postpartum	RCVS with SAH
8	674.03 (1)	yes	Antepartum	TIA
9	674.04 (1)	yes	Postpartum	RCVS
10	674.04 (1)	yes	Postpartum	RCVS
11	674.04 (5)	yes	Postpartum	SAH, possible RCVS
12	674.04 (1)	yes	Postpartum	RCVS with SAH
13	674.04 (1)	yes	Postpartum	RCVS with SAH
14	674.01 (3)	no	Delivery admission	Remote AVM bleed
15	674.04 (1)	yes	Postpartum	Cortical vein thrombosis with SAH
16	674.03 (1)	no	Antepartum	Meningioma
17	674.04 (1)	yes	Postpartum	Cortical vein thrombosis, venous infarct
18	674.02 (8)	yes	Postpartum	ICH/SAH
19	674.04 (1)	yes	Postpartum	Basilar occlusion
20	674.04 (1)	yes	Postpartum	ICA occlusion
21	674.03 (1)	yes	Antepartum	AVM rupture, ICH
22	674.03 (5)	yes	Antepartum	R MCA cryptogenic stroke
23	674.03 (1)	yes	Antepartum	AVM rupture, ICH
24	674.04 (1)	yes	Antepartum	AVM rupture, ICH
25	674.04 (1)	yes	Postpartum	RCVS with SAH
26	674.01 (2)	no	Delivery admission	Chronic hypertension
27	674.04 (1)	yes	Postpartum	Cardioembolic stroke

28	674.01 (2)	no	Delivery admission	Remote ICH from cavernous malformation
29	674.01 (1)	no	Delivery admission	Remote aneurysmal SAH
30	674.04 (1)	yes	Postpartum	ICH
31	674.04 (1)	yes	Postpartum	RCVS with ICH
32	674.04 (1)	yes	Postpartum	RCVS
33	674.01 (2)	yes	Postpartum	Recurrent RCVS
34	674.03 (1)	no	Antepartum	Unruptured aneurysm
35	674.04 (1)	yes	Postpartum	RCVS with TIA
36	674.03 (1)	no	Antepartum	Complicated migraine
37	674.02 (5)	yes	Postpartum	RCVS with ICH
38	674.01 (2)	yes	Antepartum	AVM rupture, ICH
39	674.01 (1)	yes	Antepartum	Cryptogenic stroke
40	674.02 (5)	yes	During delivery	Cardioembolic stroke
41	674.04 (1)	yes	Postpartum	RCVS with SAH
42	674.03 (1)	yes	Antepartum	Cryptogenic strokes
43	674.01 (8)	no	Delivery admission	Known moyamoya
44	674.02 (7)	yes	Postpartum	RCVS with SAH
45	674.01 (1)	no	Delivery admission	Unruptured aneurysm
46	674.01 (1)	no	Delivery admission	Unruptured AVM
47	674.03 (1)	yes	Antepartum	RCVS
48	674.02 (5)	yes	Postpartum	RCVS
49	674.01 (1)	yes	Antepartum	AVM rupture, ICH
50	674.01 (1)	yes	Postpartum	TIA
51	674.04 (1)	yes	Postpartum	RCVS with SAH
52	674.03 (1)	yes	Antepartum	AVM rupture, ICH
53	674.03 (9)	no	Postpartum	Old gunshot wound, hemiparesis
54	674.04 (1)	yes	Postpartum	ICH
55	674.01 (1)	yes	Antepartum	Cardioembolic strokes
56	674.03 (1)	yes	Antepartum	Aneurysmal SAH

Supplemental Table II. ICD-9 Codes Used in Identifying Patients and Patient Characteristics

Patient characteristics	CODES (ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification)
IDENTIFICATION OF DELIVERIES AND PREGNANCY CHARACTERISTICS	
Antepartum admission	Admissions with pregnancy code (630-648) with no delivery code;[7] fifth digit of 3 in codes for pregnancy-related primary or secondary diagnosis; V22, V23, V28, or 792.3 for any listed diagnosis; antenatal DRG codes 378–384 [8]
Delivery admission	Admissions with delivery code (vaginal or cesarean delivery, see below)[7]
Postpartum admission	Admissions with postpartum code (660-677) with no delivery code OR APR/DRG 561;[7] fifth digit of 2 or 4 in pregnancy-related codes for primary or secondary diagnosis; code V24 for any listed diagnosis; or postpartum DRG codes 376–377[8]
Postpartum stroke during delivery admission	Admissions with delivery code AND pregnancy-associated stroke code with suffix .x2 (fifth digit "2")[9]
Vaginal delivery	V27, 72.x, 73.x, 650–659, APR/DRG 541, 560[10]
Cesarean delivery	74.0x-74.2x, 74.4, 74.9x, 669.70, 669.71, 762.1, 763.4 or APR/DRG 540[11]
Peripartum hemorrhage	666[4]
Gestational hypertension	642.3x, 642.9x[12]
Mild or unspecified preeclampsia[a]	642.4x, 642.7x[13]
Severe preeclampsia[a]	642.5x[13]
Eclampsia[a,b]	642.6x[13]
Multiple gestation	V27.2-V27.8, 651.x[11]
Proteinuria/nephrotic syndrome	791.0, 581.81[9]
Gestational diabetes	648.8x[11]
Small for gestational age	656.5x[10]
Assisted reproductive technology	V23.85[9]
History of previous cesarean section	654.2x[12]
Primagravida	V22.0, V23.81, V23.83[9]
Multigravida	V22.1, V23.82, V23.84[9]
Grand multiparity (5 or more deliveries)	V23.3, 659.40, 659.41, 659.43[9]
Stillbirth	656.4x, V27.1, V27.3, V27.4, V27.6, V27.7[11]

[a]These codes were shown to have PPV of 94.5% when applied to inpatient hospitalizations[13]	
[b]For the severity-stratified analysis, "eclampsia" was included in the "severe" group due to a validation study showing that more than half of women given this code did not meet criteria for eclampsia; all the women in the validation study misclassified as "eclampsia" met criteria for "severe preeclampsia" as defined until the 2013 update by the American College of Obstetricians and Gynecologists.[14,15]	
VASCULAR RISK FACTORS	
Sickle cell disease	282.4x, 282.6x[11,12]
Systemic lupus erythematosus	710.0x[11,12]
Coagulopathy	286.0-286.9, 287.1, 287.3-287.5, 289.81-289.82[16]
Hypercoagulable state	289.81, 289.82,[17] 649.3x[9]
DVT/PE (acute, chronic, or history of prior)	415.1x, 453.4x, 453.5x, 453.72, 453.74, 453.75, 453.76, 453.77, 453.82, 453.84, 453.85, 453.86, 453.87, 671.3x, 671.4x, 673.0x, 673.1x, 673.2x, 673.3x, 673.8x, V12.51, V12.55[9]
Chronic renal disease	581.x-583.x, 585.x, 587.x, 588.x, 646.2x[11,12]
Active smoking	305.1.x, 649.0x[12]
Preexisting hypertension	401.x-405.x, 642.0x-642.2x, 642.7x[11]
Diabetes mellitus (excluding gestational diabetes)	250.x, 648.0x[11,12]
Obesity	278.0x, 649.1x ,V85.3, V85.4[12]
Migraine	346.x[7]
Malignancy	140.x-208.x[11]
Pulmonary hypertension	416.0, 416.8, 416.9[11,12]
Chronic ischemic heart disease	412.x-414.x[11,12]
Congenital heart disease	745.0x-747.4x, 648.5x[11,12]
Valvular heart disease	394.x-397.x, 424.x[11,12]
Congestive heart failure	428.22, 428.23, 428.32, 428.33, 428.42, 428.43[12]
Drug abuse or dependence	304.x-305.0x, 305.2x-305.9x, 648.3x[11,12]
Alcohol abuse	291.xx, 303.xx, 305.0x[12]
INFECTIONS[9]	
Pregnancy-related (includes the following):	
Postpartum infection	670x, 672x[4]
Chorioamnionitis	658.4x[11]
Infectious and parasitic conditions in the mother classifiable elsewhere but complicating pregnancy childbirth or the puerperium	647.xx

Mastitis	675.xx
Puerperial infections	670.0x, .1x, .8x
Sexually transmitted (includes the following):	
HIV	HIV-specific flag in SPARCS database
Syphilis	647.0x
Gonorrhea	647.1x
Other venereal	647.2x
Trichomoniasis	131.xx
Sexually transmitted infections	091.xx - 099.xx
Herpes simplex	054.xx
Respiratory (includes the following):	
Acute nasopharyngitis	460
Acute sinusitis	461.x
Acute pharyngitis	462
Acute laryngitis and tracheitis	464.xx
Acute upper respiratory infections of multiple or unspecified sites	465.x
Chronic sinusitis	473.x
Postnasal drip	784.91
Viral pneumonia	480.x
Pneumococcal pneumonia	481
Other bacterial pneumonia	482.xx
Pneumonia due to other specified organism	483.x
Pneumonia in infectious diseases classified elsewhere	484.x
Bronchopneumonia, organism unspecified	485
Pneumonia, organism unspecified	486
Streptococcal sore throat	034.0
Whooping cough	033.xx
Abscess of lung	513.0
Tuberculosis, pulmonary	011, 012

Rheumatic pneumonia	517.1
Pulmonary coccidioidomycosis, unspecified	114.5
Primary coccidioidomycosis (pulmonary)	114.0
Infection by Histoplasma, pneumonia	115.x5
Pneumonitis due to toxoplasmosis	130.4
Pneumocystosis	136.3
Candidiasis of lung	112.4
Ornithosis with pneumonia	073.0
Postmeasles pneumonia	055.1
Varicella (hemorrhagic) pneumonitis	052.1
Pulmonary actinomycotic infection	039.1
Pulmonary tularemia	021.2
Pulmonary anthrax	022.1
Diphtheria	032.0 - 032.3, 032.84
Genitourinary (includes the following):	
Infections of kidney	590.xx
Cystitis	595.xx
Urethritis not sexually transmitted and urethral syndrome	597.xx
Urethral stricture due to infection	598.0x
Urinary tract infection	599.0
Gastrointestinal (includes the following):	
Gastrointestinal infections	001.xx - 009.xx
Sepsis (includes the following):	
Bacteremia	790.7
Sepsis	995.91
Severe sepsis	995.92
Septic shock	785.52
Septicemia	038.0, 038.1x-0.38.9x

Sepsis in pregnancy	670.2x, 670.3x
Anthrax septicemia	022.3
Meningococcemia	036.2
Herpetic septicemia	054.5
Septic arterial embolism	449
Other (includes the following):	
Cellulitis	681.xx, 682.xx, 686.xx
Lyme disease	088.81
Plague	020.2, 020.3, 020.4, 020.5
Diseases due to other mycobacteria	031.0
Q fever	083.0
Primary extrapulmonary coccidioidomycosis	114.1
ACUTE CEREBROVASCULAR DISEASE CODES (not pregnancy-specific)[1]	
Ischemic stroke	433.01, 433.10, 433.11, 433.21, 433.31, 433.81, 433.91, 434.00, 434.01, 434.11, 434.91, and 436[1]
Transient ischemic attack	435[1]
Intracerebral hemorrhage	431[1]
Subarachnoid hemorrhage	430[1]
Epidural/subdural intracranial hemorrhage	432[3]
Pituitary apoplexy	253.2[3]
Carotid/vertebral artery dissection	443.21, 443.24[3]
Cerebral venous thrombosis	325[18]
Other acute cerebrovascular disorders	437.x[19]
Iatrogenic stroke	997.02[1]
Trauma (excluded from analysis)	800-804, 850-854[3]
Acute rehabilitation admission (excluded from analysis)	V57.x
PREGNANCY-SPECIFIC STROKE CODES	
Peripartum phlebitis and thrombosis, cerebral venous thrombosis, and thrombosis of intracranial venous sinus	671.5[3,4]
Cerebrovascular disorders in the puerperium, unspecified	674[1]

Cerebrovascular disorders in the puerperium, delivered, with or without mention of antepartum condition	674.01[1]
Cerebrovascular disorders in the puerperium, delivered, with mention of postpartum complication	674.02[1]
Cerebrovascular disorders in the puerperium, antepartum condition or complication	674.03[1]
Cerebrovascular disorders in the puerperium, postpartum condition or complication	674.04[1]
References for codes are noted in table and included in Reference list at end of Supplementary Appendix. ICD-9: International Classification of Diseases, 9th edition. APR: All patient refined. DRG: diagnosis related group. PPV: positive predictive value. DVT: deep vein thrombosis. PE: pulmonary embolism. HIV: human immunodeficiency virus. SPARCS: Statewide Planning and Research Cooperative System.	

Supplemental Table III. Discharge disposition in women with preeclampsia, with and without pregnancy-associated stroke (control group matched on age, race/ethnicity, and severity of preeclampsia).

Disposition	Cases (PEC and PAS) n = 197 (%)	Controls (PEC and no PAS) n = 591 (%)
Home	89 (45.2)	540 (91.4)
Home with home services	30 (15.2)	39 (6.6)
Left against medical advice	1 (0.5)	7 (1.2)
Acute inpatient rehabilitation	23 (11.7)	1 (0.2)
Other acute care hospital	22 (11.2)	2 (0.3)
Skilled nursing facility	6 (3.0)	1 (0.2)
Death (in hospital)*	26 (13.2)	1 (0.2)

*There was no significant difference in mortality between stroke cases with mild and severe PEC; 7 of 57 (12.3%) of mild cases died, and 19 of 140 (13.6%) severe cases died (p=0.81). The majority of women who died had hemorrhagic strokes (21 of 26, 80.1%). More deaths were due to hemorrhagic stroke in the severe group than in the mild group (89.5% vs 57.1%, p=0.06), although the difference did not reach statistical significance.

Supplemental Table IV. Subgroup analysis, mild and severe cases/controls, univariable analysis

	Mild Group			Severe group			Matched on Severity		
Prevalence of risk factors	Cases (PAS)	Controls (without PAS)	p-value	Cases (PAS)	Controls (without PAS)	p-value	Cases (PEC and PAS)	Controls (PEC without PAS)	p-value
	n=57 (%)	n=171 (%)		n=140 (%)	n=420 (%)		N = 197 (%)	N (591)	
Pre-existing hypertension	25 (44)	35 (20)	p=0.001	19 (14)	9 (2)	p<0.0001	44 (22)	44 (7)	<.0001
Prothrombotic states	1 (2)	9 (5)	p=0.5	25 (18)	13 (3)	p<0.0001	26 (13)	22 (4)	<.0001
Hypercoagulable state	*1 (2)*	*6 (4)*	*p=0.7*	*14 (10)*	*10 (2)*	*p<0.0001*	*15 (8)*	*16(3)*	*0.002*
Sickle cell	*0 (0)*	*1 (1)*	*p=1.0*	*5 (4)*	*0 (0)*	*p<0.0001*	*5 (3)*	*1 (0)*	*0.005*
Lupus	*0 (0)*	*2 (1)*	*p=1.0*	*2 (1)*	*0 (0)*	*p=0.1*	*2 (1)*	*2 (0)*	*0.3*
DVT/PE (acute, chronic, or history of prior)	*0 (0)*	*0 (0)*		*10 (7)*	*3 (1)*	*p<0.0001*	*10 (5)*	*3 (1)*	*<.0001*
Any infection present on admission	12 (21)	9 (5)	p=0.001	16 (11)	25 (6)	p=0.04	28 (14)	34 (6)	p<0.001
Genitourinary infection	*10 (18)*	*4 (2)*	*p=0.002*	*10 (7)*	*6 (1)*	*p=0.001*	*20 (10)*	*10 (2)*	*p<0.001*
Chorioamnionitis	*0 (0)*	*4 (2)*	*p=0.6*	*4 (3)*	*8 (2)*	*p=0.5*	*4 (2)*	*12 (2)*	*p=1.0*
Non-specified pregnancy related infection	*3 (5)*	*4 (2)*	*p=0.4*	*3 (2)*	*16 (4)*	*p=0.4*	*6 (3)*	*20 (3)*	*p=1.0*
Respiratory infection	*0 (0)*	*0 (0)*		*0 (0)*	*2 (0)*	*p=1.0*	*0 (0)*	*2 (0)*	*p=1.0*
Gastrointestinal infection	*0 (0)*	*0 (0)*		*1 (1)*	*1 (0)*	*p=0.4*	*1 (1)*	*1 (0)*	*p=0.4*
Sexually transmitted infection (includes HIV)	*1 (2)*	*0 (0)*	*p=0.3*	*0 (0)*	*6 (1)*	*p=0.3*	*1 (1)*	*6 (1)*	*p=0.7*
Sepsis	*1 (2)*	*1 (1)*	*p=0.4*	*2 (1)*	*0 (0)*	*p=0.1*	*3 (2)*	*1 (0)*	*p=0.1*
Other infection	*3 (5)*	*0 (0)*	*p=0.02*	*1 (1)*	*11 (3)*	*p=0.3*	*4 (2)*	*11 (2)*	*p=1.0*
Coagulopathy	5 (9)	7 (4)	p=0.2	24 (17)	26 (6)	p<0.0001	29 (15)	33 (6)	<.0001
Migraine	3 (5)	0 (0)	p=0.02	3 (2)	5 (1)	p=0.4	6 (3)	5 (1)	0.03
Any heart disease	1 (2)	0 (0)	p=0.3	5 (4)	4 (1)	p=0.05	6 (3)	4 (1)	0.02
Congestive heart failure	*0 (0)*	*0 (0)*		*1 (1)*	*0 (0)*	*p=0.3*	*1 (1)*	*0 (0)*	*0.3*
Chronic ischemic heart disease	*0 (0)*	*0 (0)*		*1 (1)*	*0 (0)*	*p=0.3*	*1 (1)*	*0 (0)*	*0.3*
Congenital heart disease	*0 (0)*	*0 (0)*		*1 (1)*	*1 (0)*	*p=0.3*	*1 (1)*	*0 (0)*	*0.3*
Valvular heart disease	*1 (2)*	*0 (0)*	*p=0.3*	*2 (1)*	*4 (1)*	*p=0.6*	*3 (2)*	*4*	*0.4*
Chronic renal disease	0 (0)	3 (2)	p=0.6	1 (1)	2 (0)	p=1.0	1 (1)	5	1.0
Proteinuria/nephrotic syndrome	0 (0)	0 (0)		1 (1)	0 (0)	p=0.3	1 (1)	*0 (0)*	0.3
Drug abuse or dependence	1 (2)	3 (2)	p=1.0	3 (2)	7 (2)	p=0.7	4 (2)	10 (2)	0.8
Alcohol abuse	1 (2)	4 (2)	p=1.0	3 (2)	9 (2)	p=1.0	4 (2)	13 (2)	1.0
HIV/AIDS (SPARCS Indicator)	0 (0)	0 (0)		0 (0)	3 (1)	p=0.6	0 (0)	3 (1)	0.6
Diabetes	4 (7)	6 (4)	p=0.3	3 (2)	8 (2)	p=1.0	7 (4)	14 (2)	0.4
Active smoking	2 (4)	6 (4)	p=1.0	2 (1)	7 (2)	p=1.0	4 (2)	13 (2)	1.0
Obesity	6 (11)	2 (1)	p=0.004	2 (1)	13 (3)	p=0.4	8 (4)	15 (3)	0.3
Pulmonary hypertension	0 (0)	0 (0)		0 (0)	2 (0)	p=1.0	0 (0)	2 (0)	1
Gestational diabetes	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	*0 (0)*	
Gestational hypertension	2 (4)	4 (2)	p=0.6	5 (4)	16 (4)	p=0.9	7 (4)	20 (3)	1.0
Multiple gestation	1 (2)	10 (6)	p=0.3	3 (2)	31 (7)	p=0.02	4 (2)	41 (7)	0.008
Multigravida	0 (0)	0 (0)		17 (12)	134 (32)	p<0.0001	35 (18)	182	0.0004

Supplemental Table V: Demographics and risk factors: Comparing mild vs severe controls, mild vs severe cases

	Mild PEC, controls (n=171)	Severe PEC, controls (n=420)	p-value	Mild PEC, cases (n=57)	Severe PEC, cases (n=140)	p-value
Age[a]			p = 0.4			p= 0.7
24 and under	30 (17.5%)	96 (22.9%)		10 (17.5%)	32 (22.9%)	
25-34	84 (49.1%)	195 (46.4%)		28 (49.1%)	65 (46.4%)	
35-44	57 (33.3%)	129 (30.7%)		19 (33.3%)	43 (30.7%)	
Race/Ethnicity[a]			p = 0.8			p= 1.0
Non-Hispanic White	42 (24.6%)	108 (25.7%)		14 (24.6%)	36 (25.7%)	
Non-Hispanic Black	63 (36.8%)	150 (35.7%)		21 (36.8%)	50 (35.7%)	
Non-Hispanic Other	33 (19.3%)	66 (15.7%)		11 (19.3%)	22 (15.7%)	
Hispanic	30 (17.5%)	87 (20.7%)		10 (17.5%)	29 (20.7%)	
Unknown	3 (1.8%)	9 (2.1%)		1 (1.8%)	3 (2.1%)	
Insurance status[a]			p = 0.5			p= 0.6
Uninsured	3 (1.8%)	3 (0.7%)		0 (0.0%)	4 (2.9%)	
Medicare	1 (0.6%)	6 (1.4%)		14 (24.6%)	29 (20.7%)	
Medicaid	35 (20.5%)	95 (22.6%)		43 (75.4%)	105 (75.0%)	
Private	132 (77.2%)	316 (75.2%)		0 (0.0%)	2 (1.4%)	
Multigravida	48 (28.1%)	134 (31.9%)	p = 0.4	18 (31.6%)	17 (12.1%)	p=0.001
Multiple gestation	10 (5.8%)	31 (7.4%)	p = 0.5	1 (1.8%)	3 (2.1%)	p=1.0
Cesarean section	92 (53.8%)	306 (72.9%)	p < 0.0001	34 (59.6%)	85 (60.7%)	p= 0.9
Any infection present on admission (includes the following)	9 (5%)	26 (6%)	p=0.8	12 (21%)	16 (11%)	p=0.1
Genitourinary infection	*4 (2)*	*6 (1%)*	*p=0.3*	*10 (6%)*	*10 (7%)*	*p=0.2*
Chorioamnionitis	*4 (2)*	*8 (2)*	*p=0.8*	*0 (0%)*	*4 (3%)*	*p=0.3*
Non-specified pregnancy related infection	*4 (2%)*	*16 (5%)*	*p=0.5*	*3 (5%)*	*3 (2%)*	*p=0.4*
Respiratory infection	*0 (0%)*	*2 (0%)*	*p=1.0*	*0 (0%)*	*0 (0%)*	
Gastrointestinal infection	*0 (0%)*	*1 (0%)*	*p=1.0*	*0 (0%)*	*1 (1%)*	*p=1.0*

Sexually transmitted infection (includes HIV)	*0 (0%)*	*6 (1%)*	*p=0.2*	*1 (2%)*	*0 (0%)*	*p=0.3*
Sepsis	*1 (1%)*	*0 (0%)*	*p=0.3*	*1 (2%)*	*2 (1%)*	*p=1.0*
Other infection	*0 (0%)*	*11 (3%)*	*p=0.04*	*3 (5%)*	*1 (1%)*	*p=0.1*
Diabetes	6 (3.5%)	8 (1.9%)	p = 0.2	4 (7.0%)	3 (2.1%)	p=0.1
Pre-existing hypertension	35 (20.5%)	9 (2.1%)	p < 0.0001	25 (43.9%)	19 (13.6%)	P<0.0001
Any heart disease[b]	0 (0%)	4 (1.0%)	p = 0.3	1 (1.8%)	5 (3.6%)	p=0.7
Migraine	0 (0%)	5 (1.2%)	p = 0.3	3 (5.3%)	3 (2.1%)	p=0.4
Obesity	2 (1.2%)	13 (3.1%)	p = 0.3	6 (10.5%)	2 (1.4%)	p=0.01
Chronic renal disease	3 (1.8%)	2 (0.5%)	p = 0.1	0 (0.0%)	1 (0.7%)	p=1.0
Prothrombotic state[c]	9 (5.3%)	13 (3.1%)	p = 0.2	1 (1.8%)	25 (17.9%)	p=0.002
History of or presence of deep venous thrombosis or pulmonary embolism	0 (0%)	3 (0.7%)	p = 0.6	0 (0.0%)	10 (7.1%)	p=0.1
Lupus	2 (1.2%)	0 (0%)	p = 0.1	0 (0.0%)	2 (1.4%)	p=1.0
Primary hypercoagulable state	6 (3.5%)	10 (2.4%)	p = 0.4	1 (1.8%)	14 (10.0%)	p=0.1
Sickle cell disease	1 (0.6%)	0 (0%)	p = 0.3	0 (0.0%)	5 (3.6%)	p=0.3
Coagulopathy	7 (4.1%)	26 (6.2%)	p = 0.4	5 (8.8%)	24 (17.1%)	p=0.2
Pulmonary hypertension	0 (0%)	2 (0.5%)	p = 1.0	0 (0%)	0 (0%)	
Active smoking	6 (3.5%)	7 (1.7%)	p = 0.2	2 (3.5%)	2 (1.4%)	p=0.6
Drug abuse or dependence	3 (1.8%)	7 (1.7%)	p = 1.0	1(1.8%)	3 (2.1%)	p=1.0
Alcohol abuse	4 (2.3%)	9 (2.1%)	p = 1.0	1(1.8%)	3 (2.1%)	p=1.0
HIV/AIDS	0 (0%)	3 (0.7%)	p = 0.6	0 (0%)	0 (0%)	

[a] p-values refer to significance of distribution across categories.
[b] "Any heart disease" includes congenital or valvular heart disease, congestive heart failure, or chronic ischemic heart disease.
[c] "Prothrombotic state" includes history of or current deep venous thrombosis or pulmonary embolism, lupus, primary hypercoagulable states, or sickle cell disease.

Supplemental Table VI. Stroke risk factors in cases and controls (matched on age, race/ethnicity, and severity), excluding cases and controls with eclampsia

Risk factors: multivariable analysis (excluding eclampsia)		Odds ratio	95% CI
Chronic hypertension	Unadjusted	4.1	2.3-7.4
	Adjusted	**4.2**	**2.2-7.8**
Infection present on admission	Unadjusted	4.2	2.2-8.1
	Adjusted	**3.7**	**1.8-7.7**
Prothrombotic states	Unadjusted	3.4	1.8-6.4
	Adjusted	**2.6**	**1.1-6.3**
Multiple gestation	Unadjusted	0.3	0.1-0.9
	Adjusted	**0.2**	**0.06-0.8**
Heart disease	Unadjusted	3.6	1.0-13.4
	Adjusted	1.4	0.3-6.6
Multigravida	Unadjusted	0.7	0.4-1.1
	Adjusted	0.8	0.5-1.3
Coagulopathy	Unadjusted	3.2	1.7-6.0
	Adjusted	1.7	0.7-4.0

Supplemental Table VII. Subgroup Analysis: Post-partum cases only

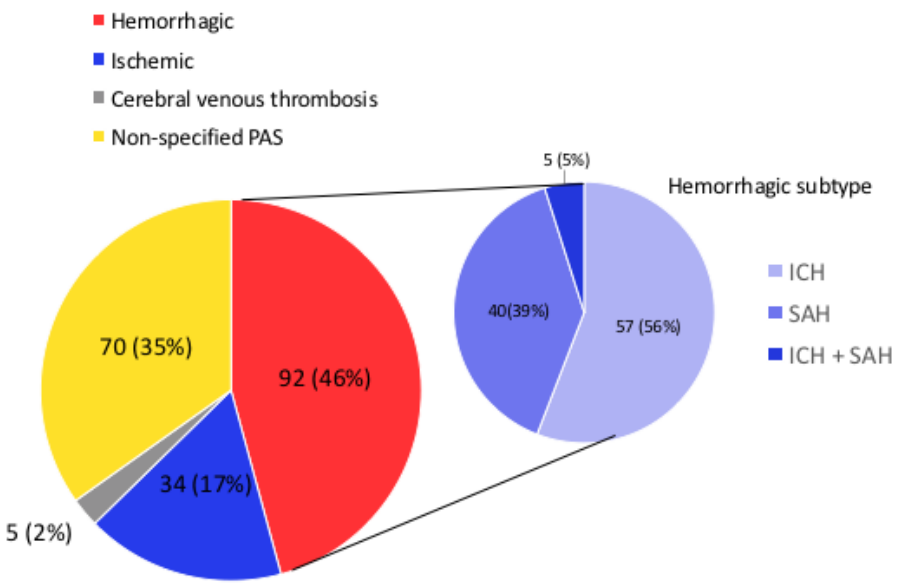
Risk factors, postpartum cases and their controls: univariate analysis	Cases (PEC and postpartum PAS)	Controls (PEC without PAS)	p-value
	n=131 (%)	n=393 (%)	
Chronic hypertension	**30 (23)**	**27 (7)**	**p<0.0001**
Prothrombotic states	**18 (14)**	**13 (3)**	**p<0.0001**
Hypercoagulable state	*9 (7)*	*10 (3)*	*p=0.03*
Sickle cell	*2 (2)*	*0 (0)*	*p=0.1*
Lupus	*1 (1)*	*1 (0)*	*p=0.4*
DVT/PE (acute, chronic, or history of prior)	*7 (5)*	*2 (1)*	*p=0.001*
Any infection present on admission	**22 (18)**	**22 (6)**	**p<0.0001**
Genitourinary infection	*18 (14)*	*4 (1)*	*p<0.0001*
Chorioamnionitis	*3 (2)*	*9 (2)*	*p=1.0*
Non-specified pregnancy related infection	*4 (3)*	*15 (4)*	*p=0.8*
Respiratory infection	*0 (0)*	*2 (1)*	*p=1.0*
Gastrointestinal infection	*0 (0)*	*1 (0)*	*p=1.0*
Sexually transmitted infection (includes HIV)	*0 (0)*	*4 (1)*	*p=0.6*
Sepsis	*2 (2)*	*1 (0)*	*p=0.2*
Other infection	*2 (2)*	*8 (2)*	*p=1.0*
Coagulopathy	**16 (12)**	**19 (5)**	**p=0.003**
Migraine	**4 (3)**	**2 (1)**	**p=0.04**
Any heart disease	**5 (4)**	**2 (1)**	**p=0.01**
Congestive heart failure	*1 (1)*	*0 (0)*	*p=0.25*
Chronic ischemic heart disease	*0 (0)*	*0 (0)*	
Congenital heart disease	*3 (2)*	*2 (1)*	*p=0.2*
Valvular heart disease	*1 (1)*	*0 (0)*	*p=0.25*
Chronic renal disease	0 (0)	3 (1)	p=0.6
Proteinuria/nephrotic syndrome	1 (1)	0 (0)	p=0.25
Drug abuse or dependence	1 (1)	6 (2)	p=0.7
Alcohol abuse	2 (2)	6 (2)	p=1.0
HIV/AIDS (SPARCS Indicator)	0 (0)	2 (1)	p=1.0
Diabetes	4 (3)	9 (2)	p=0.7
Active smoking	3 (2)	9 (2)	p=1.0
Obesity	3 (2)	11 (3)	p=1.0
Pulmonary hypertension	0 (0)	1 (0)	p=1.0
Gestational diabetes	0 (0)	0 (0)	
Gestational hypertension	4 (3)	12 (3)	p=1.0
Multiple gestation	**1 (1)**	**24 (6)**	**p=0.01**
Multigravida	**18 (14)**	**122 (31)**	**p=0.0001**
Cesarean section	**68 (52)**	**254 (65)**	**p=0.002**

PEC: preeclampsia. PAS: pregnancy-associated stroke. DVT: deep vein thrombosis. PE: pulmonary embolism. Bolded characteristics were included in the multivariable model.

Supplemental Table VIII. Stroke risk factors in post-partum cases and their controls (matched on age, race/ethnicity, and severity)

Risk factors: multivariable analysis		**Odds ratio**	**95% CI**
Chronic hypertension	Unadjusted	5.6	2.8-11.0
	Adjusted	**5.0**	**2.3-10.5**
Infection present on admission	Unadjusted	3.6	1.9-6.9
	Adjusted	**3.6**	**1.8-7.3**
Prothrombotic states	Unadjusted	4.4	2.1-9.1
	Adjusted	**3.6**	**1.4-9.7**
Coagulopathy	Unadjusted	2.8	1.4-5.6
	Adjusted	1.3	0.5-3.5
Heart disease	Unadjusted	7.5	1.5-38.7
	Adjusted	3.7	0.4-33.4
Multiple gestation	Unadjusted	0.1	0.02-0.9
	Adjusted	0.1	0.01-1.0
Multigravida	Unadjusted	0.4	0.2-0.6
	Adjusted	**0.4**	**0.2-0.7**
Cesarean section	Unadjusted	0.6	0.4-0.9
	Adjusted	0.7	0.4-1.1

Supplemental Figure I: Stroke subtypes in women with preeclampsia and stroke



There were 197 women identified during the study period with preeclampsia and stroke of any type. The large circle indicates stroke types (ischemic, hemorrhagic, cerebral venous thrombosis or non-specified), with raw numbers and percentage of total cases. The smaller circle indicates the subtypes of hemorrhagic stroke in shades of blue, with raw numbers and percentages within the group of women with hemorrhagic strokes. Of the 92 women with hemorrhagic strokes, 11 (12.0%) had underlying coagulopathies and 12 (13.0%) had underlying prothrombotic states. Among women with ischemic strokes, 6 of 34 (17.6%) had coagulopathies, and another 6 of 34 (17.6%) had prothrombotic states; in non-specified PAS, 12 of 70 (17.1%) had coagulopathies, and 8 of 70 (11.4%) had prothrombotic states. PAS: pregnancy-associated stroke. ICH: intracerebral hemorrhage. SAH: subarachnoid hemorrhage.

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