

Title: **Association between neonatal uterine bleeding and endometriosis-related symptoms later in life**

Authors: Kanae Ogawa¹, Khaleque N Khan^{1*}, Haruo Kuroboshi¹, Akemi Koshiba¹, Go Horiguchi², Satoshi Teramukai², Akira Fujishita³, Kyoko Itoh⁴, Sun-Wei Guo⁵, Jo Kitawaki¹, Taisuke Mori¹

Suppl. Table 1A. Logistic regression analyses (Outcome: A1 “Do you feel pain during period (cyclic)?”)

Variables		Outcome: A1*		Univariate			Multivariate (n=81)		
		Yes (n=77)	No (n=6)	Odds ratio	[95%CI]	P value	Odds ratio	[95%CI]	P value
NUB	-	50 (96.2)	2 (3.8)	ref			ref		
	+	27 (87.1)	4 (12.9)	0.27	[0.05, 1.57]	0.145	0.34	[0.05, 2.37]	0.276
Age (years)		22 (20-26)	22 (20-25)	0.96	[0.56, 1.67]	0.892	0.73	[0.38, 1.39]	0.333
Body height (cm)		160 (147-174)	156 (153.7-159)	1.17	[0.96, 1.42]	0.121	1.07	[0.89, 1.28]	0.484
Body weight (kg)	NA	1	1						
		51.8 (41-82)	52 (46-72)	0.95	[0.87, 1.04]	0.285			
BMI (kg/m ²)	NA	1	1						
		19.9 (15.8-31.2)	21.7 (18.9-29.6)	0.80	[0.63, 1.01]	0.065	0.74	[0.54, 1.01]	0.053
Age at menarche (years)	NA	1	1						
		12 (8-16)	11.5 (11-13)	1.19	[0.65, 2.15]	0.574	0.85	[0.46, 1.57]	0.595
Family history of cyclic pain	No	16 (94.1)	1 (5.9)	ref					
	Yes	34 (97.1)	1 (2.9)	2.13	[0.13, 36.2]	0.602			
	NA	27	4						
Family history of acyclic pain	No	33 (91.7)	3 (8.3)	ref					
	Yes	14 (100)	0 (0)	3.03	[0.13, 68.9]	0.487			
	NA	30	3						
Gestational age at delivery (week)		39 (37-41)	40.5 (39-43)	0.27	[0.10, 0.75]	0.012	0.77	[0.29, 2.06]	0.600
Maternal age at delivery (years)		32 (24-42)	27 (25-35)	1.39	[1.04, 1.85]	0.026	1.37	[1.02, 1.84]	0.039
Birth weight (100g)		30.30 (22.16-40.66)	29.66 (27.10-37.24)	0.95	[0.76, 1.18]	0.618	0.97	[0.74, 1.26]	0.817
Normal menstrual cycle	No	13 (92.9)	1 (7.1)	ref					
	Yes	56 (91.8)	5 (8.2)	0.86	[0.09, 8.01]	0.896			
	NA	8	0						
Menstrual lag ≥ 7 days	No	62 (92.5)	5 (7.5)	ref			ref		
	Yes	15 (93.8)	1 (6.2)	1.21	[0.13, 11.1]	0.867	1.32	[0.08, 21.2]	0.846
Bleeding period ≥ 8 days	No	71 (92.2)	6 (7.8)	ref			ref		
	Yes	6 (100)	0 (0)	1.18	[0.05, 29.3]	0.919	0.54	[0.02, 16.8]	0.723

Suppl. Table 1B. Logistic regression analyses (Outcome: A2 “Do you feel pain beyond period (acyclic)?”)

Variables		Outcome: A2*		Univariate			Multivariate (n=49)		
		Yes (n=36)	No (n=47)	Odds ratio	[95%CI]	P value	Odds ratio	[95%CI]	P value
NUB	-	28 (53.8)	24 (46.2)	ref			ref		
	+	8 (25.8)	23 (74.2)	0.30	[0.11, 0.79]	0.015	0.75	[0.19, 2.93]	0.681
Age (years)		22 (20-26)	22 (20-25)	1.22	[0.91, 1.63]	0.194	1.15	[0.72, 1.83]	0.566
Body height (cm)		158.7 (150-170.5)	160 (147-174)	0.96	[0.88, 1.05]	0.381	0.95	[0.83, 1.09]	0.453
Body weight (kg)	NA	1	1						
		51.5 (43-64)	52 (41-82)	0.97	[0.91, 1.03]	0.271			
BMI (kg/m ²)	NA	1	1						
		20.0 (15.8-27.3)	19.9 (16.6-31.2)	0.95	[0.81, 1.11]	0.490	0.88	[0.68, 1.15]	0.354
Age at menarche (years)	NA	1	1						
		12 (8-16)	12 (9-16)	0.90	[0.66, 1.22]	0.488	0.75	[0.44, 1.28]	0.288
Family history of cyclic pain	No	8 (47.1)	9 (52.9)	ref					
	Yes	16 (45.7)	19 (54.3)	0.95	[0.30, 3.03]	0.927			
	NA	12	19						
Family history of acyclic pain	No	12 (33.3)	24 (66.7)	ref			ref		
	Yes	10 (71.4)	4 (28.6)	5.00	[1.30, 19.3]	0.020	6.59	[1.07, 40.4]	0.042
	NA	14	19						
Gestational age at delivery (week)		39 (37-41)	40 (37-43)	0.65	[0.43, 0.99]	0.044	0.82	[0.39, 1.73]	0.593
Maternal age at delivery (years)		32 (25-42)	32 (24-40)	1.07	[0.96, 1.18]	0.217	1.08	[0.91, 1.28]	0.392
Birth weight (100g)		29.62 (22.16-36.72)	30.94 (25.16-40.66)	0.86	[0.75, 0.98]	0.024	0.87	[0.70, 1.07]	0.188
Normal menstrual cycle	No	4 (28.6)	10 (71.4)	ref					
	Yes	26 (42.6)	35 (57.4)	1.86	[0.52, 6.58]	0.338			
	NA	6	2						
Menstrual lag ≥ 7 days	No	29 (43.3)	38 (56.7)	ref			ref		
	Yes	7 (43.7)	9 (56.3)	1.02	[0.34, 3.06]	0.973	1.56	[0.23, 10.7]	0.649
Bleeding period ≥ 8 days	No	32 (41.6)	45 (58.4)	ref			ref		
	Yes	4 (66.7)	2 (33.3)	2.81	[0.49, 16.3]	0.249	0.82	[0.07, 10.2]	0.878

Suppl. Table 1C. Logistic regression analyses (Outcome: A4 “Degree of your cyclic pain (VAS score)”)

Variables		Outcome: A4*		Univariate			Multivariate (n=81)		
		7-10 (n=30)	0-6 (n=53)	Odds ratio	[95%CI]	P value	Odds ratio	[95%CI]	P value
NUB	-	20 (38.5)	32 (61.5)	ref			ref		
	+	10 (32.3)	21 (67.7)	0.76	[0.30, 1.95]	0.570	0.71	[0.22, 2.32]	0.572
Age (years)		22 (20-25)	22 (20-26)	1.13	[0.84, 1.53]	0.413	1.16	[0.80, 1.67]	0.445
Body height (cm)		160 (147-170.5)	159 (151-174)	0.96	[0.88, 1.05]	0.408	0.99	[0.89, 1.10]	0.884
Body weight (kg)	NA	1	1						
		52 (41-82)	51.4 (41-79)	1.01	[0.96, 1.07]	0.705			
BMI (kg/m ²)	NA	1	1						
		20.9 (16.6-29.6)	19.9 (15.8-31.2)	1.07	[0.91, 1.25]	0.418	0.97	[0.80, 1.18]	0.792
Age at menarche (years)	NA	1	1						
		12 (8-14)	12 (10-16)	0.85	[0.61, 1.16]	0.300	0.66	[0.43, 1.02]	0.063
Family history of cyclic pain	No	6 (35.3)	11 (64.7)	ref					
	Yes	16 (45.7)	19 (54.3)	1.54	[0.47, 5.11]	0.477			
	NA	8	23						
Family history of acyclic pain	No	12 (33.3)	24 (66.7)	ref					
	Yes	6 (42.9)	8 (57.1)	1.50	[0.42, 5.32]	0.530			
	NA	12	21						
Gestational age at delivery (week)		40 (37-41)	39 (37-43)	1.37	[0.91, 2.08]	0.137	2.08	[1.12, 3.86]	0.020
Maternal age at delivery (years)		33 (25-42)	31 (24-41)	1.10	[0.98, 1.22]	0.096	1.09	[0.96, 1.24]	0.170
Birth weight (100g)		30.40 (23.38-40.66)	30.30 (22.16-37.50)	1.00	[0.88, 1.13]	0.963	0.96	[0.82, 1.12]	0.588
Normal menstrual cycle	No	5 (35.7)	9 (64.3)	ref					
	Yes	21 (34.4)	40 (65.6)	0.95	[0.28, 3.18]	0.927			
	NA	4	4						
Menstrual lag ≥ 7 days	No	21 (31.3)	46 (68.7)	ref			ref		
	Yes	9 (56.2)	7 (43.8)	2.82	[0.92, 8.58]	0.069	6.96	[1.46, 33.2]	0.015
Bleeding period ≥ 8 days	No	27 (35.1)	50 (64.9)	ref			ref		
	Yes	3 (50.0)	3 (50.0)	1.85	[0.35, 9.81]	0.469	0.92	[0.10, 8.75]	0.944

Suppl. Table 1D. Logistic regression analyses (Outcome: A5 “Degree of your acyclic pain (VAS score)”)

Variables		Outcome: A5*		Univariate			Multivariate (n=49)		
		7-10 (n=10)	0-6 (n=73)	Odds ratio	[95%CI]	P value	Odds ratio	[95%CI]	P value
NUB	-	7 (13.5)	45 (86.5)	ref			ref		
	+	3 (9.7)	28 (90.3)	0.69	[0.16, 2.89]	0.610	1.35	[0.21, 8.55]	0.753
Age (years)		22.5 (21-24)	22 (20-26)	1.13	[0.73, 1.75]	0.581	1.16	[0.61, 2.20]	0.647
Body height (cm)		156 (150-163)	160 (147-174)	0.86	[0.74, 1.00]	0.050	0.83	[0.67, 1.02]	0.074
Body weight (kg)	NA	1	1						
		54 (44-64)	51.4 (41-82)	1.03	[0.95, 1.11]	0.514			
BMI (kg/m ²)	NA	1	1						
		22.2 (18.1-27.3)	19.9 (15.8-31.2)	1.19	[0.97, 1.46]	0.094	1.07	[0.82, 1.39]	0.646
Age at menarche (years)	NA	1	1						
		11 (8-14)	12 (9-16)	0.53	[0.30, 0.93]	0.027	0.74	[0.40, 1.38]	0.348
Family history of cyclic pain	No	2 (11.8)	15 (88.2)	ref					
	Yes	5 (14.3)	30 (85.7)	1.25	[0.22, 7.22]	0.803			
	NA	3	28						
Family history of acyclic pain	No	3 (8.3)	33 (91.7)	ref			ref		
	Yes	4 (28.6)	10 (71.4)	4.40	[0.84, 23.0]	0.079	2.32	[0.26, 20.9]	0.452
	NA	3	30						
Gestational age at delivery (week)		40 (37-40)	39 (37-43)	0.96	[0.54, 1.71]	0.883	1.00	[0.36, 2.79]	0.997
Maternal age at delivery (years)		32 (25-42)	32 (24-41)	1.01	[0.86, 1.17]	0.943	1.02	[0.84, 1.25]	0.826
Birth weight (100g)		30.12 (22.16-33.94)	30.30 (23.38-40.66)	0.89	[0.73, 1.08]	0.235	1.03	[0.79, 1.34]	0.822
Normal menstrual cycle	No	1 (7.1)	13 (92.9)	ref					
	Yes	6 (9.8)	55 (90.2)	1.42	[0.16, 12.8]	0.756			
	NA	3	5						
Menstrual lag ≥ 7 days	No	7 (10.4)	60 (89.6)	ref			ref		
	Yes	3 (18.8)	13 (81.2)	1.98	[0.45, 8.69]	0.366	2.20	[0.24, 20.6]	0.489
Bleeding period ≥ 8 days	No	8 (10.4)	69 (89.6)	ref			ref		
	Yes	2 (33.3)	4 (66.7)	4.31	[0.68, 27.4]	0.121	2.48	[0.12, 50.3]	0.555

Suppl. Table 1E. Logistic regression analyses (Outcome: A6 “Does your cyclic/acyclic pain disturb daily life activity?”)

Variables		Outcome: A6*		Univariate			Multivariate (n=40)		
		Yes (n=42)	No (n=40)	Odds ratio	[95%CI]	P value	Odds ratio	[95%CI]	P value
NUB	-	31 (59.6)	21 (40.4)	ref			ref		
	+	11 (36.7)	19 (63.3)	0.39	[0.16, 0.99]	0.048	0.41	[0.05, 3.49]	0.415
Age (years)		22 (20-25)	22 (20-26)	1.14	[0.85, 1.53]	0.390	2.67	[1.01, 7.06]	0.047
Body height (cm)		160 (147-174)	159 (152-170)	0.95	[0.88, 1.04]	0.278	0.89	[0.73, 1.10]	0.282
Body weight (kg)	NA	1	1						
		52.6 (41-70)	51.3 (43-82)	1.00	[0.95, 1.06]	0.919			
BMI (kg/m ²)	NA	1	1						
		21.1 (16.6-27.3)	19.9 (15.8-31.2)	1.05	[0.90, 1.23]	0.539	1.07	[0.77, 1.49]	0.671
Age at menarche (years)	NA	1	1						
		12 (8-14)	12 (9-16)	0.78	[0.57, 1.07]	0.119	0.80	[0.37, 1.70]	0.554
Family history of cyclic pain	No	5 (29.4)	12 (70.6)	ref			ref		
	Yes	22 (62.9)	13 (37.1)	4.06	[1.16, 14.2]	0.028	2.29	[0.27, 19.7]	0.452
	NA	15	15						
Family history of acyclic pain	No	11 (31.4)	24 (68.6)	ref			ref		
	Yes	11 (78.6)	3 (21.4)	8.00	[1.85, 34.5]	0.005	8.30	[0.53, 129.9]	0.132
	NA	20	13						
Gestational age at delivery (week)		39 (37-41)	39.5 (37-43)	0.71	[0.47, 1.06]	0.093	1.30	[0.46, 3.66]	0.615
Maternal age at delivery (years)		32.5 (25-42)	30.5 (24-41)	1.08	[0.97, 1.19]	0.177	0.86	[0.70, 1.06]	0.147
Birth weight (100g)		30.17 (22.16-40.66)	30.65 (23.82-37.50)	0.96	[0.85, 1.08]	0.454	1.04	[0.83, 1.31]	0.719
Normal menstrual cycle	No	4 (28.6)	10 (71.4)	ref			ref		
	Yes	31 (51.7)	29 (48.3)	2.67	[0.75, 9.47]	0.128	3.79	[0.24, 60.3]	0.345
	NA	7	1						
Menstrual lag ≥ 7 days	No	33 (50.0)	33 (50.0)	ref			ref		
	Yes	9 (56.2)	7 (43.8)	1.29	[0.43, 3.86]	0.654	10.1	[0.46, 219.6]	0.142
Bleeding period ≥ 8 days	No	38 (50.0)	38 (50.0)	ref			ref		
	Yes	4 (66.7)	2 (33.3)	2.00	[0.35, 11.6]	0.439	0.21	[0.01, 5.85]	0.356

Suppl. Table 1F. Logistic regression analyses (Outcome: A8 “Do you take any pain killer or hormonal therapy for your cyclic pain?”)

Variables		Outcome: A8*		Univariate			Multivariate (n=73)		
		Yes (n=58)	No (n=24)	Odds ratio	[95%CI]	P value	Odds ratio	[95%CI]	P value
NUB	-	35 (67.3)	17 (32.7)	ref			ref		
	+	23 (76.7)	7 (23.3)	1.60	[0.57, 4.45]	0.372	2.40	[0.67, 8.63]	0.179
Age (years)		22 (20-25)	22.5 (20-26)	0.91	[0.67, 1.25]	0.567	1.02	[0.69, 1.52]	0.908
Body height (cm)		159 (147-170.5)	159 (151-174)	0.98	[0.89, 1.07]	0.653	1.01	[0.90, 1.14]	0.883
Body weight (kg)	NA	1	1						
		52 (41-82)	51.3 (41-72)	1.01	[0.95, 1.08]	0.703			
BMI (kg/m ²)	NA	1	1						
		20.0 (15.8-31.2)	19.9 (17.6-29.6)	1.06	[0.89, 1.27]	0.527	1.06	[0.84, 1.32]	0.633
Age at menarche (years)		12 (8-16)	12 (10-16)	0.75	[0.54, 1.05]	0.094	0.61	[0.38, 0.97]	0.038
Family history of cyclic pain	No	12 (70.6)	5 (29.4)	ref					
	Yes	28 (80.0)	7 (20.0)	1.67	[0.44, 6.32]	0.452			
	NA	18	12						
Family history of acyclic pain	No	25 (69.4)	11 (30.6)	ref					
	Yes	12 (85.7)	2 (14.3)	2.64	[0.50, 13.8]	0.251			
	NA	21	11						
Gestational age at delivery (week)		39 (37-41)	39 (37-43)	0.85	[0.56, 1.30]	0.457	1.04	[0.56, 1.91]	0.904
Maternal age at delivery (years)		32 (24-42)	32 (25-41)	1.06	[0.95, 1.19]	0.326	1.10	[0.96, 1.27]	0.174
Birth weight (100g)		30.39 (22.16-40.66)	29.78 (26.12-37.24)	0.97	[0.85, 1.10]	0.625	0.92	[0.78, 1.08]	0.306
Normal menstrual cycle	No	6 (42.9)	8 (57.1)	ref			ref		
	Yes	44 (73.3)	16 (26.7)	3.67	[1.10, 12.2]	0.034	6.31	[1.26, 31.6]	0.025
	NA	8	0						
Menstrual lag ≥ 7 days	No	47 (71.2)	19 (28.8)	ref			ref		
	Yes	11 (68.8)	5 (31.2)	0.90	[0.27, 2.91]	0.846	2.78	[0.44, 17.7]	0.279
Bleeding period ≥ 8 days	No	54 (71.1)	22 (28.9)	ref			ref		
	Yes	4 (66.7)	2 (33.3)	0.82	[0.14, 4.78]	0.820	0.55	[0.06, 4.77]	0.591