

Postnatal cardiovascular morbidity following preterm pre-eclampsia: an observational study.

Laura Ormesher^{1,2}, Suzanne Higson³, Matthew Luckie³, Stephen A Roberts⁴, Heather

Glossop², Andrew Trafford⁵, Elizabeth Cottrell¹, Edward D Johnstone^{1,2}, Jenny E Myers^{1,2}

1. Maternal and Fetal Health Research Centre, Division of Developmental Biology and Medicine, University of Manchester, UK
2. St Mary's Hospital, Manchester University NHS Foundation Trust, Manchester, UK
3. Manchester Heart Centre, Manchester University NHS Foundation Trust, Manchester, UK
4. Centre for Biostatistics, University of Manchester, UK
5. Division of Cardiovascular Sciences, University of Manchester, UK

Table 1: Baseline characteristics

		Interventional trial (placebo arm)	Observational trial	Total cohort
Age at enrolment		30.9 (6.6)	317. (6.5)	31.34 (6.47)
Ethnicity	White	17 (57%)	18 (46%)	35 (51%)
	Black	4 (13%)	6 (15%)	13 (19%)
	Asian	9 (30%)	11 (28%)	20 (29%)
	Other	0 (0%)	4 (10%)	1 (1%)
Booking BMI				28.8 (7.5)
Smoker in pregnancy		4 (13%)	4 (10%)	8 (12%)
Pre-existing hypertension*		6 (20%)	6 (15%)	12 (17%)
Pre-existing renal disease		0 (0%)	2 (5%)	2 (3%)
Booking sBP		116.0 (13.5)	115.3 (14.2)	115.6 (13.8)
Booking dBP		74.4 (11.1)	70.9 (11.0)	72.4 (11.1)
Diabetes		2 (7%)	2 (5%)	4 (6%)
Previous venous thromboembolism		1 (3%)	0 (0%)	1 (1%)
Primiparity		15 (50%)	22 (56%)	37 (54%)
No known pre-eclampsia risk factors†		19 (63%)	25 (64%)	44 (64%)
Multiparous with no known risk factors		3/15 (20%)	8/17 (47%)	11/32 (34%)
Multiparous with previous pre-eclampsia		5/15 (33%)	7/17 (41%)	12/32 (38%)

Frequencies: N (%).

Continuous data: mean (standard deviation).

*Diagnosed before or during the first 20 weeks of pregnancy.

†Risk factors including hypertension, renal disease, diabetes, antiphospholipid syndrome, systemic lupus erythematosus, age >40, BMI >30kg/m² or previous preeclampsia(38)

BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure.

Table 2: Pregnancy outcomes

Perinatal outcomes		
Gestation at delivery (weeks + days (days))*		35+0 (20)
Gestation at PE diagnosis (weeks + days (days))*		34+0 (26)
Infant sex	Male 41 (53%)	Female 37 (47%)
Multiple pregnancy		8 (12%)
	Singleton pregnancies (n=61)	Multiple pregnancies (n=8)
Birthweight centile*	2.9 (24.1)	21.6 (24.4)
Birthweight centile <10 th	40/61 (66%)	7/17 (41%)
Birthweight centile <3 rd	31/61 (51%)	3/17 (18%)
Delivery <34 weeks	20/61 (33%)	7/17 (41%)
NICU admission (days)*	6.5 (21)	4.5 (9)
Respiratory distress syndrome	15/58 (26%)	7/17 (41%)
Interventricular haemorrhage	3/58 (5%)	0/17 (0%)
Seizure	1/58 (1%)	0/17 (0%)
NEC	4/58 (6%)	0/17 (0%)
Adverse perinatal outcome†	19/61 (31%)	7/17 (41%)
Stillbirth	3/61 (5%)	0/17 (0%)
NND	2/61 (3%)	0/17 (0%)
Maternal outcomes		
Maximum systolic blood pressure		164.0 (11.8)
Maximum diastolic blood pressure		106.3 (9.1)
Eclampsia / HELLP syndrome		0 (0%)
Abruptio		1 (2%)
Maternal death		0 (0%)
Gestational diabetes		5 (7%)
Pre-eclampsia with severe features‡		53 (77%)
Spontaneous preterm birth		5 (7%)
Antenatal steroids for lung maturity		47 (68%)

Frequencies: N(%).

Continuous data: mean (standard deviation).

*Median (interquartile range).

†Composite perinatal outcome: respiratory distress syndrome / intraventricular haemorrhage / necrotising enterocolitis / stillbirth / neonatal death.

‡Definition of pre-eclampsia with severe features: maximum blood pressure > 160/110mmHg / progressive deterioration in alanine aminotransferase / creatinine / platelets.

PE, pre-eclampsia; C-section, Caesarean section; NICU, neonatal intensive care; RDS, respiratory distress syndrome; IVH, intraventricular haemorrhage; NEC, necrotising enterocolitis; NND, neonatal death; HELLP, haemolysis, elevated liver enzymes, and a low platelet count.

Table 3: Prevalence of cardiovascular and echocardiographic abnormalities at baseline (within 3 days of delivery), 6 weeks and 6 months postpartum.

	Baseline (n=69)	6 weeks (n=50)	6 months (n=44)
Raised TVR (>1200)	34 (49%)	45 (90%)	33 (75%)
Systolic dysfunction	14 (20%)	13 (26%)	3 (7%)
Diastolic dysfunction	58 (84%)	21 (42%)	27 (61%)
No remodelling	13 (19%)	25 (50%)	26 (59%)
Concentric remodelling	33 (48%)	20 (40%)	16 (36%)
Concentric hypertrophy	22 (32%)	5 (10%)	1 (2%)
Eccentric hypertrophy	1 (1%)	0 (0%)	1 (2%)
Requiring antihypertensives	53 (77%)	19 (38%)	15 (34%)
Requiring antihypertensives or BP>140/90mmHg	58 (84%)	24 (48%)	25 (57%)
Requiring antihypertensives or BP>140/90mmHg in the absence of pre-existing hypertension	46/57 (81%)	15/41 (37%)	16/35 (46%)

Frequencies: N (%).

Diastolic dysfunction defined using British Society of Echocardiography guideline flow chart(33).

TVR, total vascular resistance; BP, blood pressure.

Table 4: Change in postnatal echocardiography measures over time

	Baseline (n=69)	6 weeks (n=50)	6 months (n=44)	Mean difference between timepoints (95% C.I.)		
				Baseline to 6 weeks	Baseline to 6 months	6 weeks to 6 months
TVR (dyne.s ⁻¹ cm ⁻⁵)	1427 (382)	1749 (424)	1662 (486)	322* (175 - 469)	235* (72 - 397)	87 (-274 - 99)
HR (bpm)	85.3 (13.7)	75.3 (11.7)	78.2 (12.3)	-10.0* (-14.8 - -5.3)	-7.2* (-12.2 - -2.1)	2.9 (-2.1 - 7.8)
SV (mL)	73.9 (16.1)	63.1 (12.8)	64.8 (13.3)	-10.8* (-16.3 - -5.4)	-9.1* (-14.8 - -3.3)	1.7 (-3.6 - 7.1)
CO (L/minute)	6.3 (1.6)	4.7 (1.0)	5.0 (1.1)	-1.6* (-2.1 - -1.5)	-1.2* (-1.8 - -0.6)	3.2 (-1.2 - 7.6)
LVEF (%)	63 (5)	62 (4)	62 (3)	-1.1 (-2.7 - 0.5)	-1.0 (-2.5 - 0.6)	0.1 (-1.3 - 1.5)
Myocardial strain and strain rate						
LV basal strain (%)	-15.7 (3.3)	-16.3 (2.2)	-17.0 (2.5)	-0.6 (-1.7 - 0.4)	-1.3* (-2.5 - -0.2)	-0.7 (-1.6 - 0.3)
LV mid strain (%)	-18.8 (2.3)	-19.1 (1.8)	-19.7 (1.9)	-0.2 (-1.0 - 0.6)	-0.9* (-1.7 - -0.1)	-0.7 (-1.4 - 0.1)
LV apical strain (%)	-25.3 (3.8)	-24.5 (3.0)	-25.3 (2.6)	0.8 (-0.5 - 2.1)	0.1 (-1.2 - 1.4)	-0.8 (-1.9 - 0.4)
GLS (%)	-19.9 (2.4)	-20.0 (2.2)	-20.7 (1.8)	0.0 (-0.9 - 0.8)	-0.8 (-1.6 - 0.1)	-0.7 (-1.6 - 0.1)
E/A strain rate	2.19 (0.72)	2.38 (0.68)	2.21 (0.73)	0.19 (-0.07 - 0.46)	0.03 (-0.25 - 0.30)	-0.17 (-0.46 - 0.12)
Mitral inflow						
E deceleration time (ms)	192 (32)	197 (29)	189 (34)	4.9 (-6.8 - 16.5)	-3.7 (-16.5 - 9.2)	-8.5 (-21.6 - 4.6)
E/A ratio	1.22 (0.28)	1.3 (0.27)	1.24 (0.28)	0.12* (0.02 - 0.22)	0.03 (-0.08 - 0.13)	-0.09 (-0.20 - 0.02)
Mitral annular motion						
Septal peak S' velocity (m/s)	0.09 (0.02)	0.08 (0.01)	0.08 (0.01)	-0.01 (-0.02 - 0.00)	-0.01 (-0.02 - 0.00)	0.00 (0.00-0.00)
Lateral peak S' velocity (m/s)	0.10 (0.02)	0.09 (0.02)	0.09 (0.02)	0.00 (-0.01 - 0.00)	0.00 (-0.01 - 0.01)	0.00 (-0.01 - 0.01)
E/E' ratio	8.71 (2.00)	7.37 (1.68)	7.53 (1.51)	-1.35* (-2.04 - -0.66)	-1.19* (-1.89 - -0.49)	0.16 (-0.40 - 0.81)
Tricuspid valve						
TR Vmax (cm/s)	0.98 (1.17)	0.58 (0.95)	0.55 (0.97)	-0.40* (-0.80 - 0.00)	-0.43* (-0.85 - -0.01)	-0.03 (-0.42 - 0.36)
Cardiac morphology						
LVIDd (cm)	4.49 (0.45)	4.32 (0.48)	4.30 (0.42)	-0.17 (-0.34 - 0.00)	-0.18* (-0.35 - -0.01)	-0.02 (-0.20 - 0.17)
PWd (cm)	1.12 (0.19)	0.94 (0.19)	0.89 (0.17)	-0.18* (-0.25 - -0.11)	-0.23* (-0.30 - -0.16)	-0.05 (-0.13 - 0.02)
SWd (cm)	1.01 (0.18)	0.88 (0.17)	0.8 (0.16)	-0.12* (-0.19 - -0.06)	-0.13* (-0.19 - -0.06)	0.00 (-0.07 - 0.07)
LVM (g)	172.02 (48.50)	132.40 (46.79)	125.33 (39.32)	-39.62* (-57.20 - -22.04)	-46.69* (-63.96 - -29.43)	-7.07 (-24.91 - 10.77)
LVMi (g/m ²)	89.58 (18.65)	70.39 (18.73)	66.92 (15.28)	-19.19* (-26.06 - -12.32)	-22.67* (-29.33 - -16.01)	-3.47 (-10.54 - 3.59)
RWT	0.50 (0.10)	0.44 (0.10)	0.41 (0.09)	-0.06* (-0.10 - -0.03)	-0.09* (-0.12 - -0.05)	-0.02 (-0.06 - 0.02)
LAV (mL)	47.3 (14.4)	39.7 (11.3)	38.9 (10.5)	-7.7* (-12.6 - -2.8)	-8.4* (-13.5 - -3.4)	-0.8 (-5.3 - 3.8)
LAVi (mL/m ²)	24.7 (6.3)	21.2 (4.7)	20.9 (4.7)	-3.5* (-5.6 - -1.4)	-3.7* (-5.9 - -1.5)	-0.3 (-2.2 - 1.7)

Mean (standard deviation).

Variables were compared between time-points using paired t-test.

* P value < 0.05.

C.I., confidence interval; HR, heart rate; SV, stroke volume; CO, cardiac output; LVEF, left ventricular ejection fraction; LV, left ventricular; GLS; global longitudinal strain; TVR, total vascular resistance; LVIDd, LV internal diameter in diastole; PWd, posterior wall diameter in diastole; SWd, septal wall diameter in diastole; LVM, left ventricular mass; LVMi, LVM

indexed to body surface area; RWT, relative wall thickness; LAV left atrial volume; LAVi, LAV indexed to body surface area; TR Vmax, tricuspid regurgitation maximum velocity.