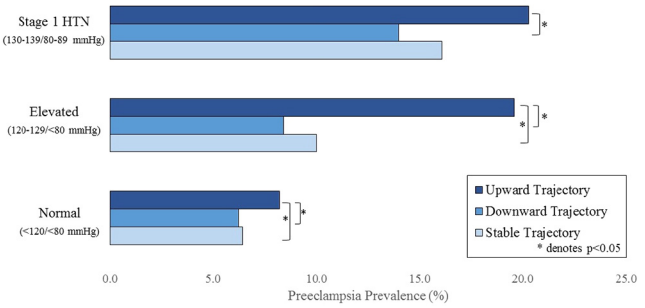
Figure. Preeclampsia Prevalence by Early Pregnancy Blood Pressure Category and Systolic Trajectory



426 Defining the gestational age cut-off between early and late preeclampsia in singletons

Amir Aviram[1,2], Jon Barrett[1,2], Arthur Zaltz[1,2], Christopher Sherman[1,2], John Kingdon[2,3], Nir Melamed[1,2]

[1]Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada, [2]University of Toronto, Toronto, Ontario, Canada, [3]Mount Sinai Hospital, Toronto, Ontario, Canada

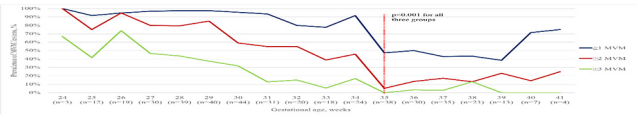
OBJECTIVE: It has been suggested that early onset preeclampsia (EPE) and late onset preeclampsia (LPE) represent two different and distinct entities. LPE is more common, and usually less severe than EPE. Yet, while these terms are widely used, there is no clear definition of the gestational age cut-off between early and late preeclampsia, and various studies named different thresholds between 32 and 36 weeks. We aimed to establish this gestational age cut-off using placental pathology, mainly maternal vascular malperfusion lesions (MVM's), which are the hallmark of placental findings in preeclampsia.

STUDY DESIGN: This was a retrospective analysis of all women with singleton gestations, at or beyond 24 weeks of gestation, diagnosed with preeclampsia, who delivered between 2001 and 2015 at a single, tertiary referral center. Placental abnormalities were classified into lesions related to maternal vascular malperfusion, fetal vascular malperfusion, lesions associated with hemorrhage and chronic inflammation. Placental findings were compared by gestational age at delivery.

RESULTS: A total of 430 women with singleton gestation and preeclampsia were eligible for analysis. Out of all of the placental pathology parameters examined, MVM's emerged as potential candidate to define the gestational age cut-off between LPE and EPE, as the prevalence of these findings decreased significantly at $35^{0/7}$ weeks of gestation (Figure). The prevalence of one or more MVM's was significantly higher $< 35^{0/7}$ weeks of gestation (93.2% vs. 47.3%, $p<0.001$) (Table). Comparing the prevalence of $\geq$2 and $\geq$3 different types of MVM's (as more sensitive markers of placental ischemia), before and after $35^{0/7}$ weeks of gestation, the same pattern was even more pronounced, (68.2% vs. 13.3%, $p<0.001$ for $\geq$2 MVM's and 33.2% vs. 3.3%, $p<0.001$ for $\geq$3 MVM's).

In a multivariable regression model, maternal age and nulliparity were not found to influence this association. In a sub-analysis of only appropriately grown neonates (birthweight>10% percentile, n=324), $35^{0/7}$ gestational weeks remained a valid threshold (91.6% vs. 37.2% for $\geq$1 MVM's, 61.6% vs. 6.6% for $\geq$2 MVM's and 28.1% vs. 1.7% for $\geq$3 MVM's, $p<0.001$ for all) (Table)

CONCLUSION: Based on the differences in the prevalence of MVM's in placental pathology specimens, the gestational age cut-off between early and late preeclampsia is $35^{0/7}$ weeks.



Variable	Preeclampsia < $35^{0/7}$ weeks (n=280)	Preeclampsia ≥ $35^{0/7}$ weeks (n=150)	p value
Maternal age, years*	32.7±6.2	34.1±5.7	0.02
Maternal age>35 years, n(%)	91 (32.5)	59 (39.3)	0.16
GA at delivery, weeks*	29 [3]	37 [3]	<0.001
Nulliparity, n(%)	159 (56.8)	105 (70.5)	0.006
HELLP syndrome, n(%)	68 (24.3)	27 (18.0)	0.13
Abruptio placenta, n(%)	3 (1.1)	4 (2.7)	0.21
Cesarean delivery, n(%)	258 (92.1)	94 (62.7)	<0.001
Birth weight, grams*	1,073 [531]	2,730 [938]	<0.001
Birthweight<10th centile, n(%)	77 (27.5)	29 (19.3)	0.06
Birthweight<5th centile, n(%)	33 (11.8)	13 (8.7)	0.32
Birthweight<3rd centile, n(%)	25 (8.9)	11 (7.3)	0.57
Male neonate, n(%)	136 (48.6)	78 (52.0)	0.50
5-minutes Apgar score<7, n(%)	36 (12.9)	7 (4.7)	0.007
UC arterial pH<7.1, n(%)	5 (1.8)	2 (1.3)	0.72
Need for resuscitation, n(%)	30 (10.7)	10 (6.7)	0.17
Admission to NICU, n(%)	273 (97.5)	38 (25.3)	<0.001
Neonatal death, n(%)	7 (3.0)	0 (0)	0.32
Placental weight, grams*	202 [92]	458 [179]	<0.001
Placental weight<10th centile, n(%)	183 (70.9)	34 (26.4)	<0.001
MVI, n(%)	170 (60.7)	92 (61.3)	0.90
Two vessel UC, n(%)	3 (1.1)	1 (0.7)	>0.99
Hypercoiled UC, n(%)	36 (12.9)	29 (19.3)	0.07
≥1 MVM, n(%)	261 (93.2)	71 (47.3)	<0.001
≥2 MVM, n(%)	191 (68.2)	20 (13.3)	<0.001
≥3 MVM, n(%)	93 (33.2)	5 (3.3)	<0.001
Placental hemorrhage, n(%)	20 (7.1)	5 (3.3)	0.11
Fetal vascular malperfusion, n(%)	79 (28.2)	37 (24.7)	0.43
Chronic villitis, n(%)	8 (2.9)	11 (7.3)	0.03
Any placental pathology, n(%)	223 (79.6)	60 (40.0)	<0.001

* Data is presented as mean±standard deviation or median [intraquartile range]
GA - Gestational age; UC - Umbilical cord; HELLP - Hemolysis, Elevated Liver enzymes and Low Platelets; NICU - Neonatal intensive care Unit; MVI - Marginal/velamentous insertion of the umbilical cord; MVM - Maternal vascular malperfusion lesion

427 Metformin decreases circulating inflammatory cytokines in a mouse model of obesity complicated by sFlt-1-induced preeclampsia

Angela R. Boyd[1], Maged Costantine[2], Katherine Jelliffe[2], Talar Kechichian[2], Phyllis Gamble[2], George Saade[2], Patrick S. Ramsey[1], Egle Bytautiene Prewit[1]

[1]The University of Texas Health Science Center San Antonio, San Antonio, TX, [2]The University of Texas Medical Branch, Galveston, TX

OBJECTIVE: Preeclampsia (PE) occurs in 3%—8% of all pregnancies and is a leading cause of maternal morbidity and mortality. Currently the only successful treatment for PE is delivery of the baby and placenta. Metformin, a biguanide medication, is used as treatment for type 2 diabetes and an acceptable oral agent for treatment of gestational diabetes. It has several mechanisms of action including targeting inflammatory, oxidative stress and vascular dysfunction pathways. Our hypothesis was that metformin reduces inflammation using an established obese mouse model of PE.

STUDY DESIGN: Female CD-1 mice were fed high fat diet for 3 months, and then mated with CD-1 male. On day 1 of gestation, mice were randomly assigned to receive metformin (300 mg/kg, MET group) in drinking water or just plain drinking water (CTR group). On day 8 of gestation mice were injected with either adenovirus vector carrying sFl1 (AdsFlt1, 109 PFU/100 μL) or mFc (AdmFc, 109 PFU/100 μL as a virus control). Mice were sacrificed on day 18 of gestation and blood was collected. The levels of IL-6, Leptin, Insulin, Plasminogen activator inhibitor -1 (PAI-1), MCP-1, and Resistin were determined using Luminex® bead array. Data were analyzed using Student t-test or Mann-Whitney test as appropriate (significance was defined as $p<0.05$).