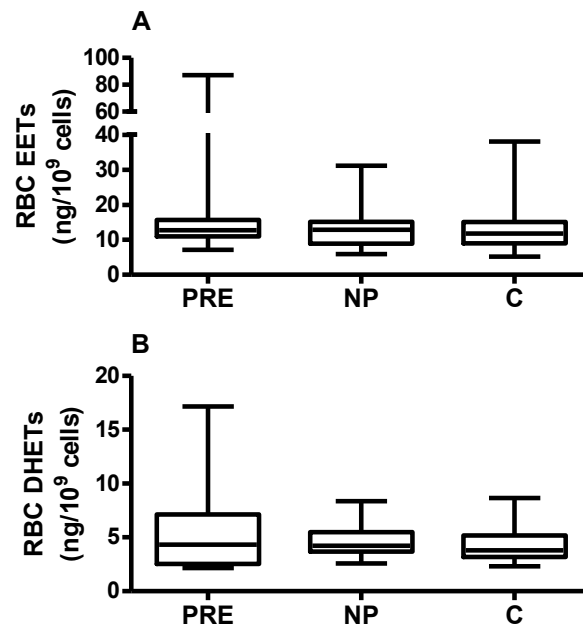
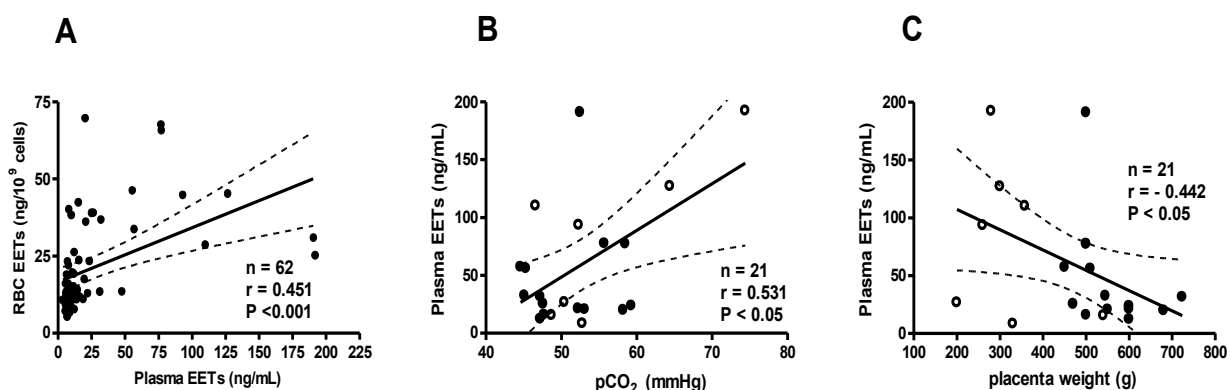


Supplementary Figure S1

Supplementary Figure S1 | Comparison of RBC eicosanoid levels in the maternal circulation (brachial artery) among preeclampsia (PRE), normal pregnancy (NP) and non-pregnant controls (C). (a) RBC EETs. (b) RBC DHETs. Values of median and range are shown (PRE, n = 19; NP, n = 29; and C, n = 19). DHETs, dihydroxyeicosatrienoic acids; EETs, epoxyeicosatrienoic acids; RBC, red blood cell.

[[change figure labels A, B, to lowercase a, b]]



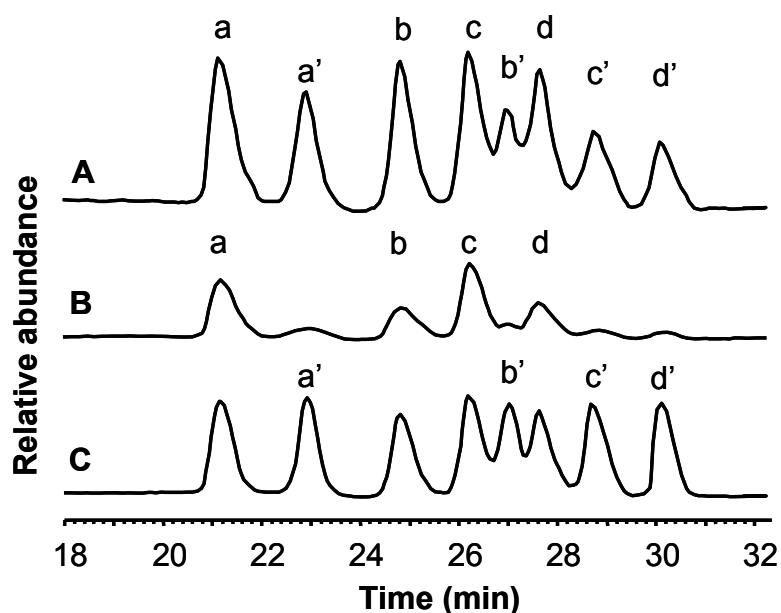
[[change to "Placenta" weight]]

[[italicize *P* and insert space either side of symbol]]

Supplementary Figure S2 | Correlation between RBC and plasma EETs and between umbilical cord venous plasma EETs and pCO₂ and placental weight.

(a) Correlation between RBC and plasma EET levels in maternal brachial and umbilical cord venous blood from normotensive and preeclamptic women. (b) Correlation between the pCO₂ and levels of umbilical cord plasma EETs. (c) Correlation between placental weight and levels of umbilical cord plasma EETs. The best-fit line and 95% confidence bands are shown. Open circles indicates umbilical cord blood or placenta from preeclamptic pregnancies. EETs, epoxyeicosatrienoic acids; r, Pearson coefficient; RBC, red blood cell.

[[change figure labels A-C to lowercase a, b, c]]



Supplementary Figure S3 | Representative LC/MS chromatogram (m/z 319) showing *cis*- and *trans*-EETs in human RBCs and plasma. (a) RBCs. (b,c) Chromatograms reflecting great variations in levels of *cis*-/*trans*-EETs in human plasma. Peaks a, b, c, and d represent 14,15-, 11,12-, 8,9-, and 5,6-*cis*-EET, while peaks a', b', c', and d' represent 14,15-, 11,12-, 8,9-, and 5,6-*trans*-EET, respectively. EETs, epoxyeicosatrienoic acids; LC/MS, liquid chromatography mass spectrometry; RBCs, red blood cells.

[[change figure labels A-C to lowercase a, b, c]]

Supplementary Information for Patients and Newborns (Table S1)

Preeclamptic women were selected according to the recommended clinical criteria: proteinuria exceeding 0.3 g/24 h and arterial blood pressure $\geq 140/90$ mmHg developing after the 20th week of gestation. To evaluate the specific role of eicosanoids in preeclampsia, patients with late-onset or preexisting hypertension; preexisting metabolic abnormalities, including diabetes mellitus, hyperlipidemia, obesity, or patients with preeclampsia complicated by HELLP (hemolysis, altered liver enzymes, low platelet count) syndrome; or any coexisting active disease were excluded.

Preeclamptic (n = 19) and a group of normotensive pregnant women (n = 19) were studied within 24 hours before delivery. Only women with single pregnancies who were scheduled for caesarean section were recruited to avoid complication by eicosanoid production during labor and parturition. Caesarean section was indicated in patients with preeclampsia because of disease progression and/or unfavorable cervical ripening. The indications for caesarean section in uncomplicated pregnancies were breech presentation, peripartum ultrasonographic diagnosis of macrosomia causing mechanical disproportion, previous caesarean section, and patient's request. Because preeclampsia is an indication for anticipated delivery, an additional group of normotensive pregnant women (n = 10) was enrolled and studied weeks before delivery to match the gestational age of the preeclamptic patients. At the time of evaluation, all preeclamptic women were receiving antihypertensive therapy according to the recommendations for the management of preeclampsia (<http://guidance.nice.org.uk/CG107>) consisting of labetalol (n = 17), slow-release nifedipine (n = 10), or alpha methyldopa (n = 3). Low-dose aspirin was taken by some preeclamptic women at the time of the study (n = 5). None of the preeclamptic women and nonpregnant controls were active smokers, whereas in the normal pregnancy group, there were three active smokers (<10 cigarettes per day).

None of the pregnant women were in active labor or had ruptured membranes or clinical signs of infection at the time of delivery. The weight of placenta and newborn were recorded.

Healthy nonpregnant controls were from the medical staff of our institutions or their relatives, and not affected by any disease on the basis of their medical history, biochemical profile, and physical examination. All studied subjects were matched for age and had a normal body mass index.

Table S1 | Clinical indices of newborns

Variable	Preeclampsia (n = 7)	Normal pregnancy (n = 14)
Weight of newborn, g	2006.0 ± 293.6**	3091.0 ± 105.8
Weight of placenta, g	324.0 ± 40.8**	552.8 ± 25.0
pH artery	7.28 ± 0.02*	7.32 ± 0.01
pH vein	7.32 ± 0.01**	7.37 ± 0.01
pCO ₂ , mmHg artery	55.7 ± 3.8	51.0 ± 1.4
pCO ₂ , mmHg vein	49.5 ± 1.3*	42.0 ± 1.6
Hemoglobin artery, g/dL	16.1 ± 0.6	14.6 ± 0.5
Hemoglobin vein, g/dL	16.5 ± 0.7	14.8 ± 0.5
Glucose artery, mg/dL	48.6 ± 4.7	52.3 ± 1.6
Glucose vein, mg/dL	59.5 ± 7.2	61.2 ± 1.4

Data are mean ± SEM; **P* < 0.05 and ***P* < 0.01 vs. normal pregnancy. Blood gases and biochemical values are those recorded at the time of delivery. Samples of blood from the umbilical cord were collected when written, informed consent was given by the pregnant women.

Supplementary Table S2 | EETs, DHETs, and 20-HETE in RBCs (ng/10⁹ cells) of umbilical cord and brachial venous blood in normotensive and preeclamptic pregnancies

	Umbilical cord	Brachial vein
Total EETs		
Preeclampsia (n = 7)	37.7 ± 3.0*	11.9 ± 0.8
Normotensive pregnancy (n = 14)	35.9 ± 4.4**	13.4 ± 1.4
Total DHETs		
Preeclampsia (n = 7)	10.2 ± 1.7*	4.5 ± 0.9
Normotensive pregnancy (n = 14)	11.2 ± 1.2**	5.3 ± 0.5
Total 20-HETE		
Preeclampsia (n = 7)	0.10 ± 0.01**	0.04 ± 0.01
Normotensive pregnancy (n = 14)	0.14 ± 0.03*	0.08 ± 0.01
Plasma (ng/mL)		
	Umbilical cord	Brachial vein
Total EETs		
Preeclampsia (n = 7)	82.0 ± 25.8	18.9 ± 5.2
Normotensive pregnancy (n = 14)	47.3 ± 12.5**	11.0 ± 0.8
Total DHETs		
Preeclampsia (n = 7)	24.5 ± 6.7*	15.1 ± 2.9
Normotensive pregnancy	24.2 ± 3.7**	13.2 ± 1.6

(n = 14)

Total 20-HETE

Preeclampsia (n = 7)

0.55 ± 0.10

0.53 ± 0.11

Normotensive pregnancy

0.54 ± 0.04**

0.34 ± 0.03

(n = 14)

Values are mean ± SEM; ** $P < 0.01$, * $P < 0.05$ vs. maternal plasma.

20-HETE, 20-hydroxyeicosatetraenoic acid; DHETs, dihydroxyeicosatrienoic acids; EETs, epoxyeicosatrienoic acids, RBCs, red blood cells.