

Marqueurs biologiques et pré éclampsie : qu'en attendre en 2012?

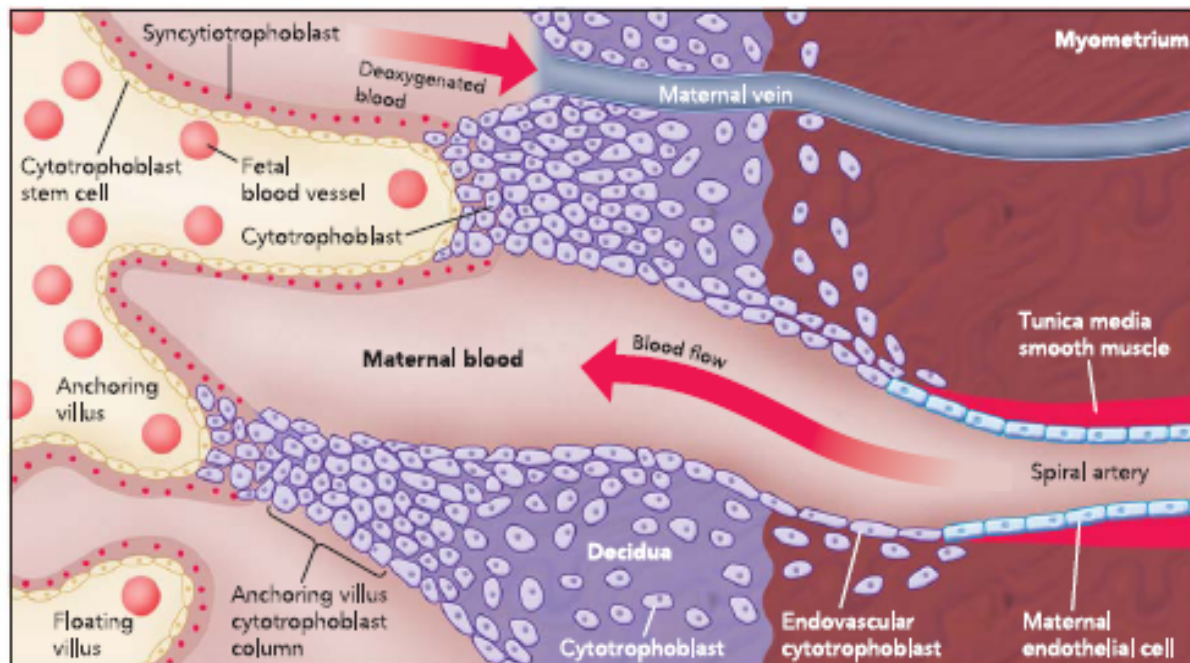
T. Pottecher, M. Sczozt
(Strasbourg)

DÉCLARATION DE LIEN D'INTÉRÊT

Je déclare avoir les liens d'intérêt suivants :

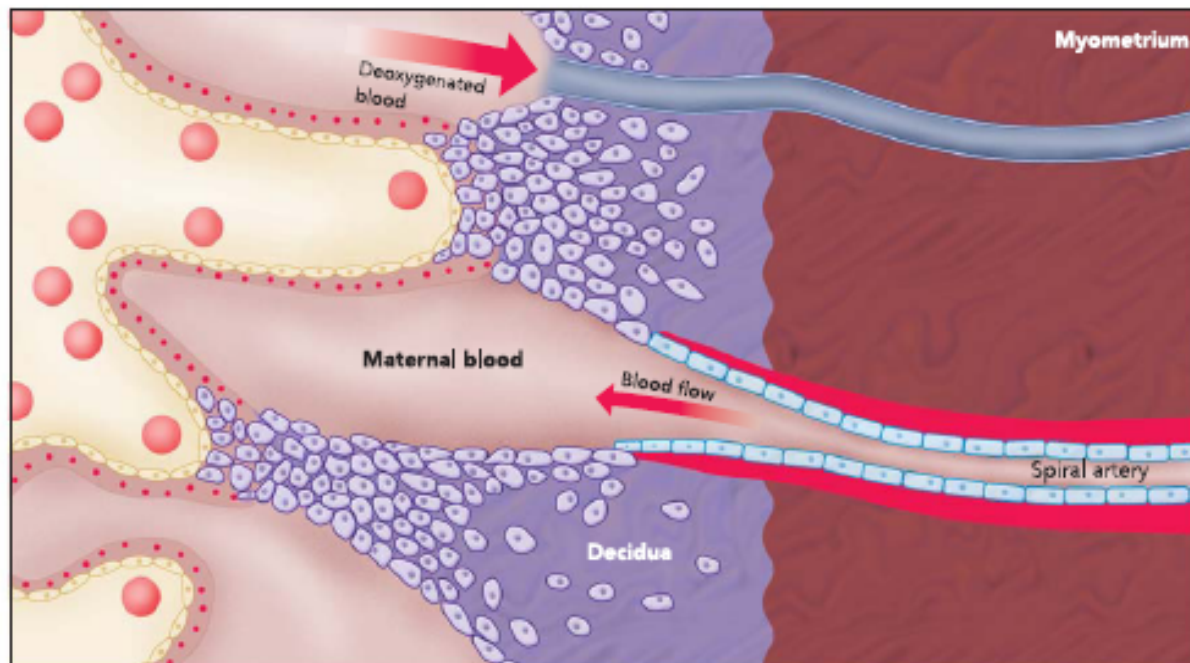
Néant

Normal

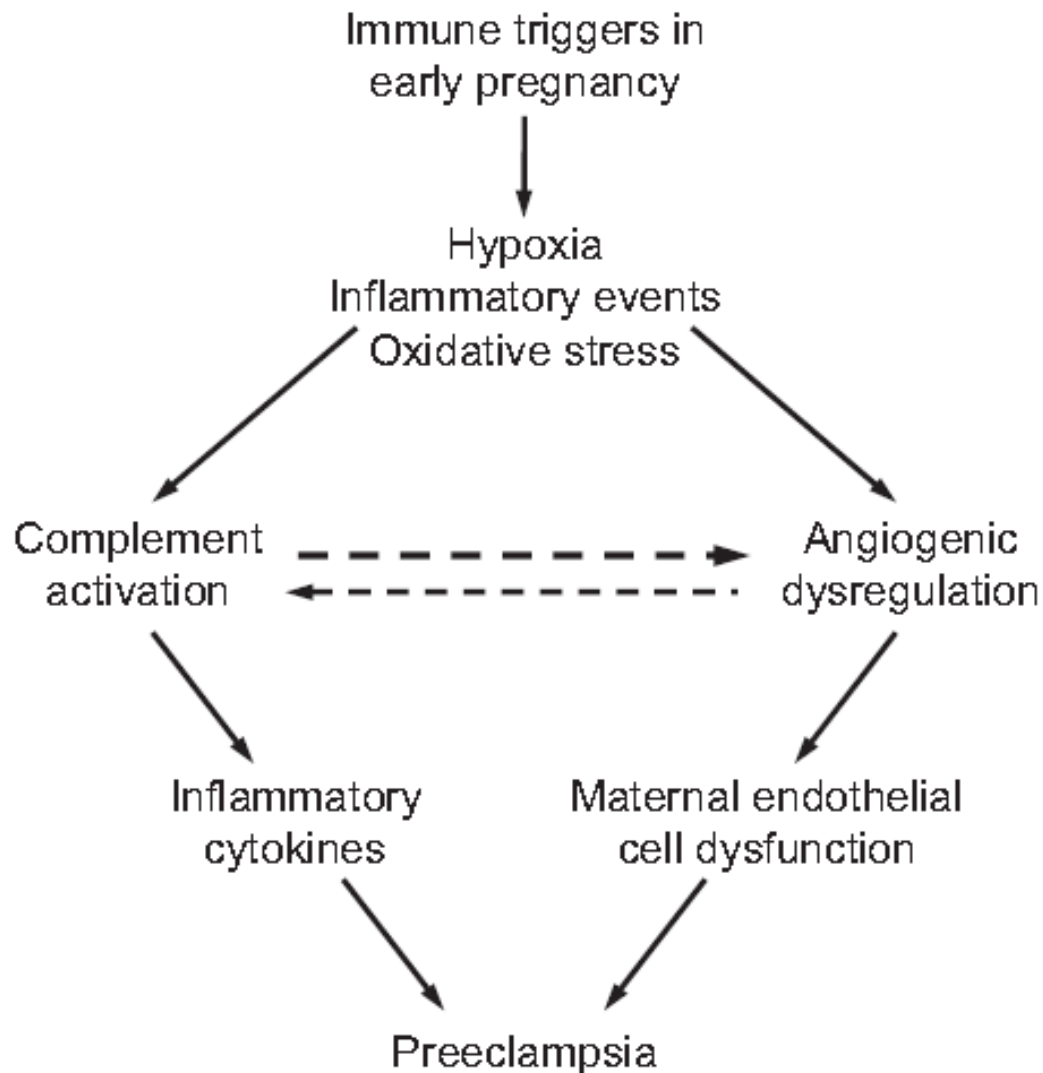


Le problème

Preeclampsia



Les conséquences : Physiopathologie schématique



Les marqueurs d'usage courant

What is already known on this topic

Spot protein to creatinine ratio has been shown to correlate well with 24 hour urinary protein estimation

A cut-off value of 30 mg/mmol (0.27) has been suggested as a reasonable "rule-out test" for proteinuria above 0.3 g/day

What this study adds

The optimum threshold for the spot protein to creatinine ratio to detect proteinuria >0.3 g/day is between 0.30 and 0.35, giving summary sensitivity and specificity values above 0.75

Insufficient evidence exists for determination of how protein to creatinine ratio should be used in clinical practice, owing to large heterogeneity in diagnostic accuracy and prevalence across studies

Insufficient evidence exists regarding the test accuracy of the albumin to creatinine ratio in pregnancy

RESEARCH

Diagnostic accuracy of spot urinary protein and albumin to creatinine ratios for detection of significant proteinuria or adverse pregnancy outcome in patients with suspected pre-eclampsia: systematic review and meta-analysis



OPEN ACCESS

R K Morris *NIHR clinical lecturer in maternal and fetal medicine*², R D Riley *reader in biostatistics*³, M Doug *research associate*¹, J J Deeks *professor of biostatistics, director of Birmingham Clinical Trials Unit*³, M D Kilby *professor of maternal and fetal medicine and honorary consultant*²

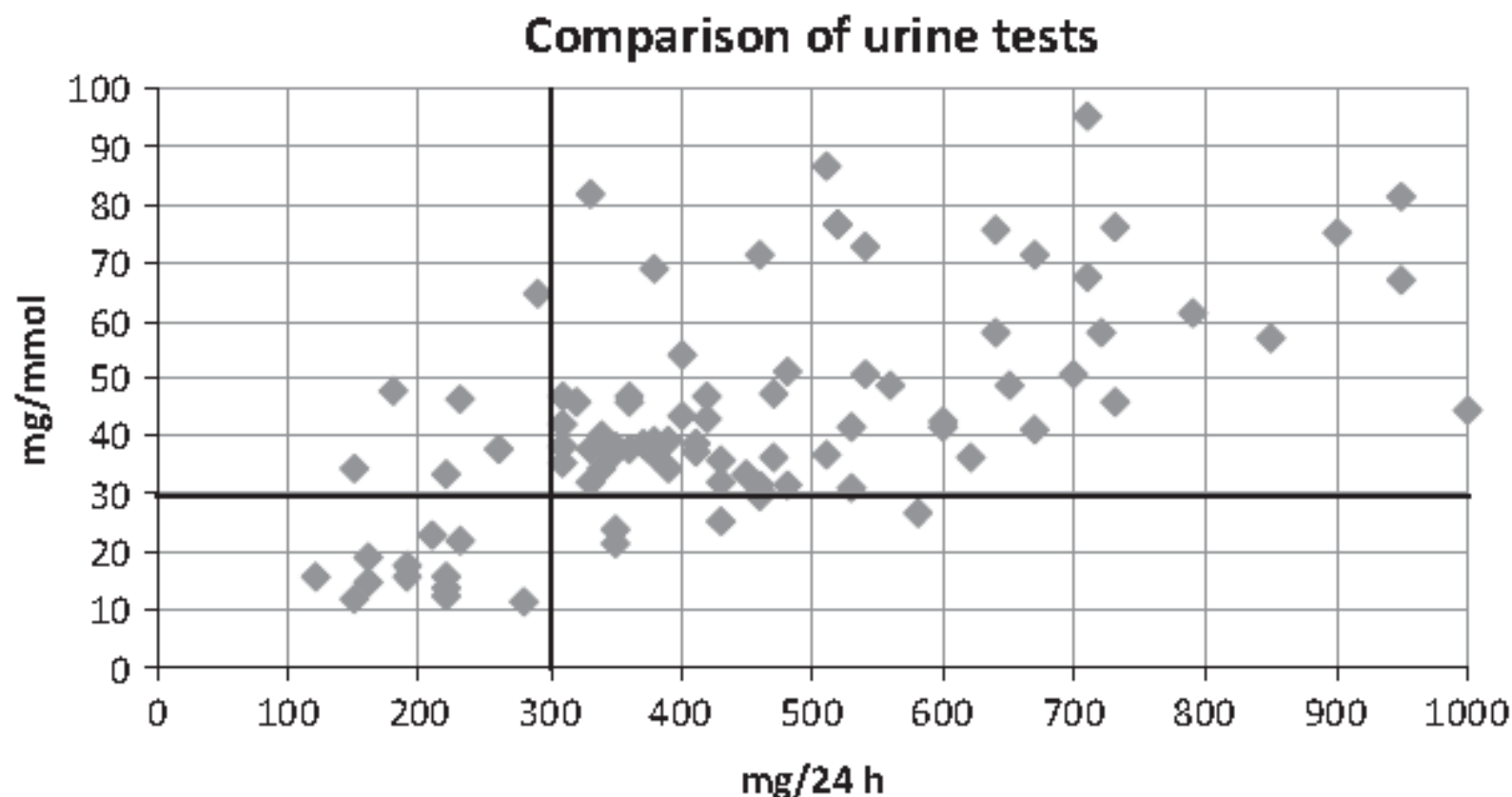
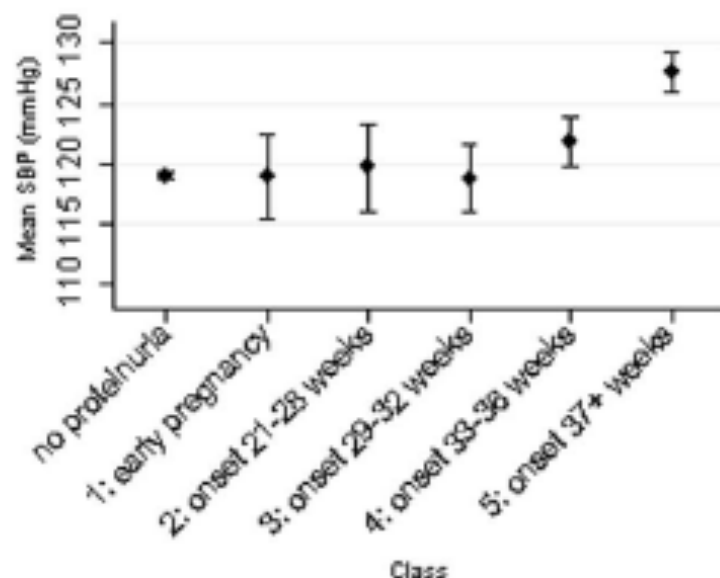


Figure 1 Individual 24-h protein versus spot urine PCR values.

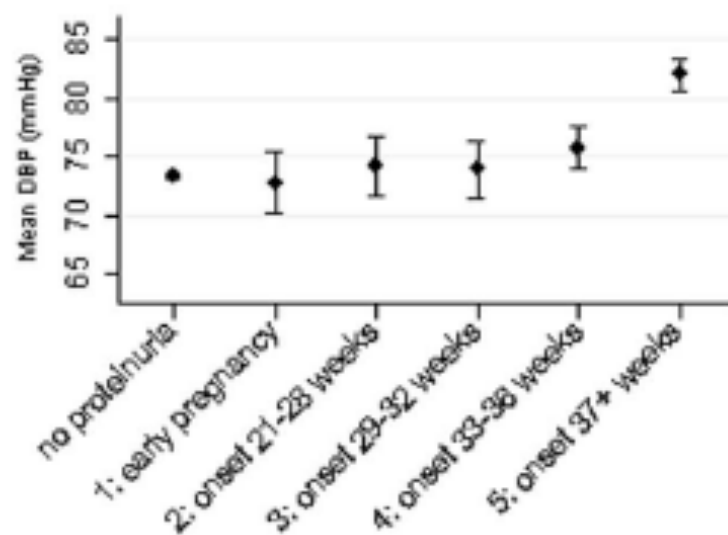
Table 1 Comparison of results of spot urine PCR and 24 h collection

	24 h collection	
	Positive	Negative
Spot urine PCR		
Positive	98	6
Negative	5	12

b) Systolic Blood Pressure at End of Pregnancy



d) Diastolic Blood Pressure at End of Pregnancy



OPEN ACCESS Freely available online

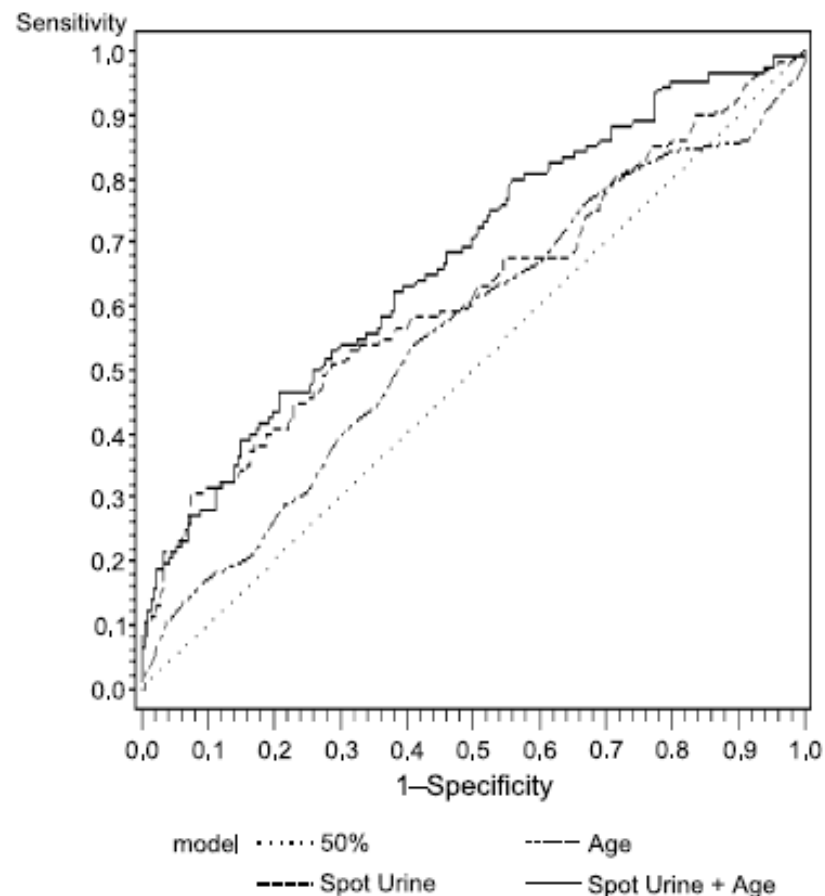
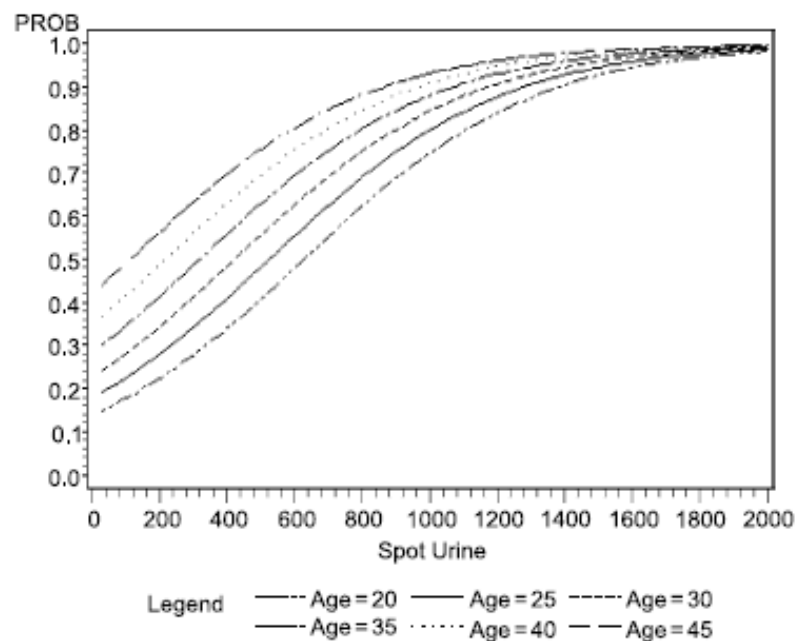
PLoS one

Relationships of Risk Factors for Pre-Eclampsia with Patterns of Occurrence of Isolated Gestational Proteinuria during Normal Term Pregnancy

Corrie Macdonald-Wallis^{1*}, Debbie A. Lawlor¹, Jon Heron², Abigail Fraser¹, Scott M. Nelson³, Kate Tilling²

July 2011 | Volume 6 | Issue 7 | e22115

Détection des complications de la pré éclampsie par le spot urinaire

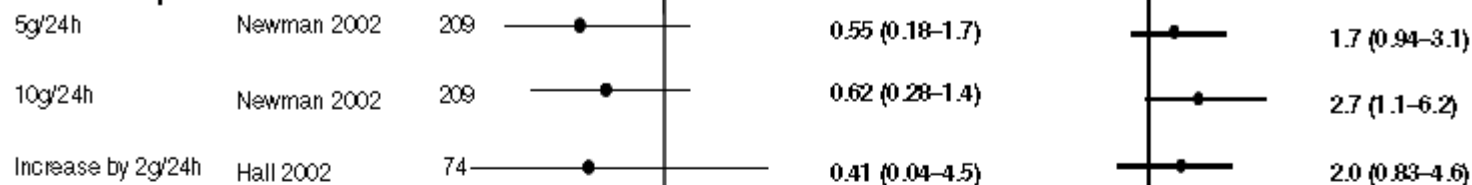


Proteinuria in pre-eclampsia: how much matters?

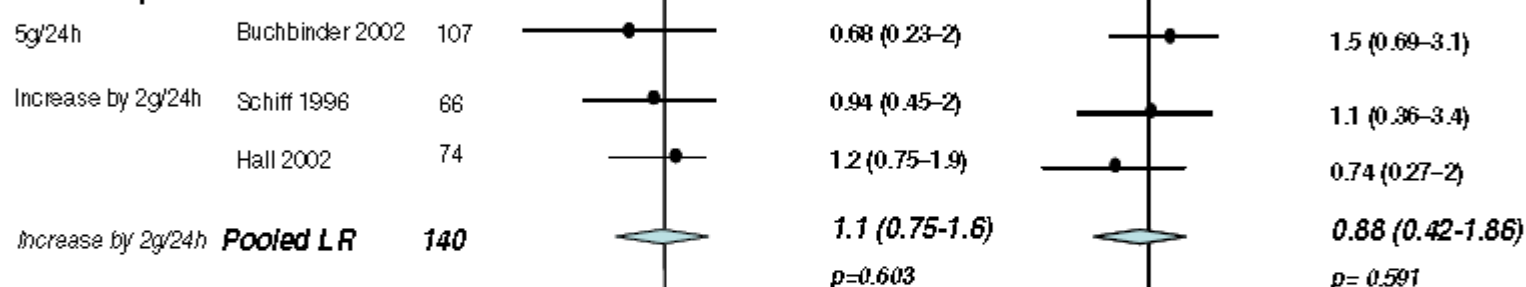
Patricia Chan,^a Mark Brown,^b Judy M. Simpson,^c Gregory Davis^a

Cut off	Study Year	Number	LR- (95% CI)	LR+ (95% CI)
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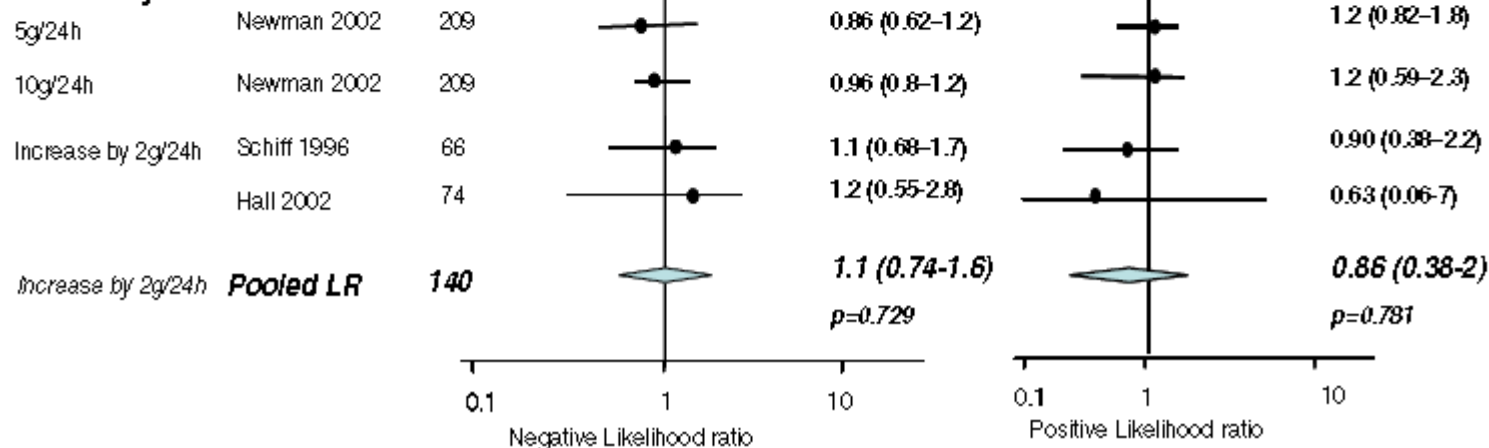
Eclampsia



Abruption



HELLP syndrome



BMC Medicine

BioMed Central

Research article

Estimation of proteinuria as a predictor of complications of pre-eclampsia: a systematic review

Shakila Thangaratinam¹, Arri Coomarasamy¹, Fidelma O'Mahony², Steve Sharp³, Javier Zamora⁴, Khalid S Khan¹ and Khaled MK Ismail²

Open Access

Protéinurie et complications maternelles

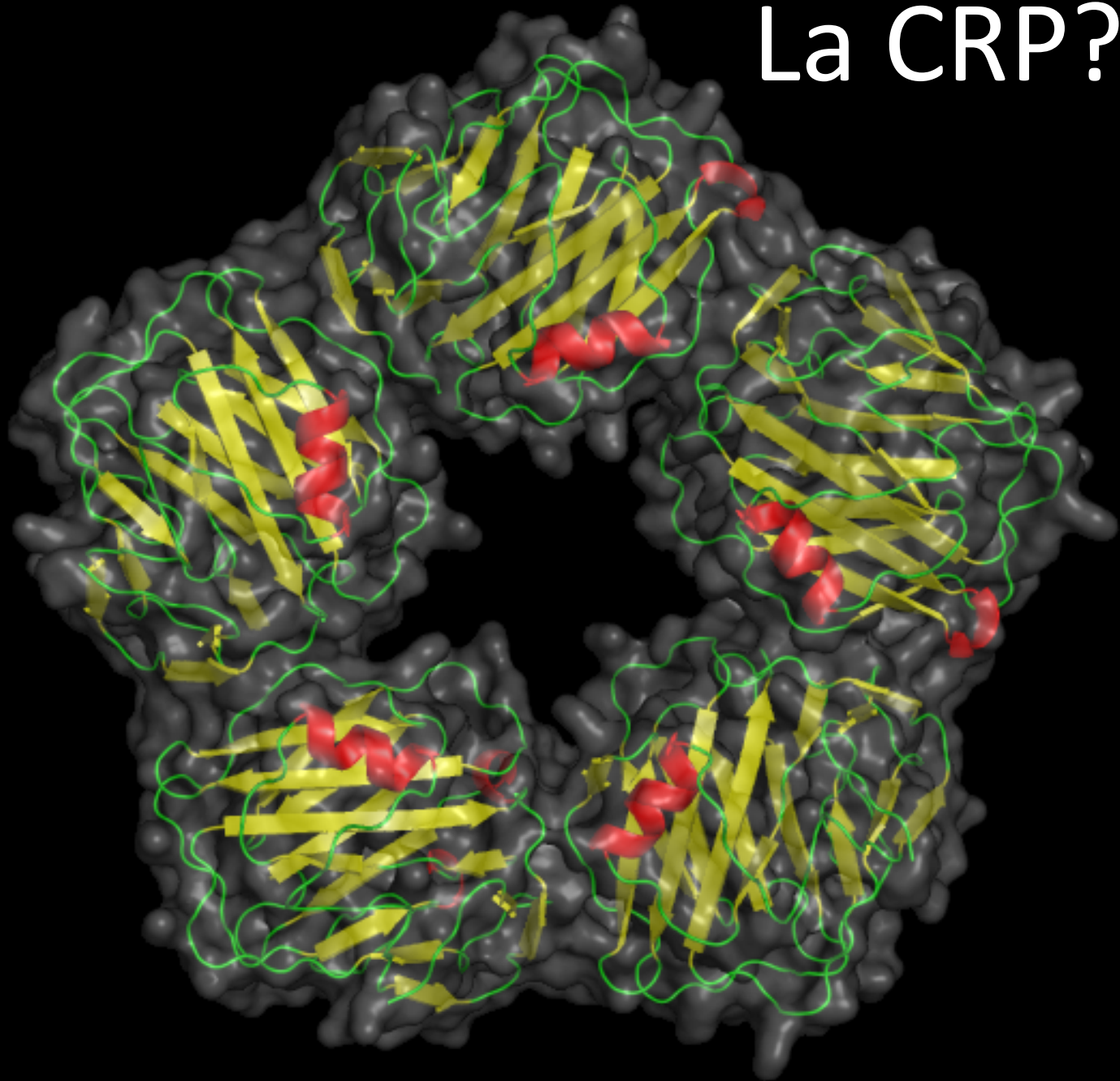
Table 3. Key relationships between uric acid and maternal or fetal outcomes

	Entire cohort (n = 1880)	
	Hyper-uricaemia	Corr hyper-uricaemia
Final diagnosis of pre-eclampsia	2.1 (1.6 2.7)*	1.9 (1.3 3.0)*
Composite adverse maternal outcomes	1.6 (1.3 2.0)*	2.0 (1.5 2.6)*
Composite adverse fetal outcomes	1.4 (1.1 1.8)*	2.2 (1.7 3.0)*
Renal dysfunction (reduced GFR)	5.6 (2.4 13.0)*	6.0 (2.1 17.3)*
Maternal thrombocytopenia	5.5 (1.6 19.6)*	3.4 (0.9 12.5)
SGA (<10th centile)	1.4 (1.0 2.0)	2.0 (1.3 3.0)*
Prematurity (<37 weeks)	1.4 (1.0 2.0)	3.1 (2.0 4.7)*

L' uricémie.....

Please cite this paper as: Hawkins T, Roberts J, Mangos G, Davis G, Roberts L, Brown M. Plasma uric acid remains a marker of poor outcome in hypertensive pregnancy: a retrospective cohort study. BJOG 2012;119:484–492.

La CRP?...



	Controls n = 115	Mild PE n = 63	Severe PE n = 34
Age (year) (mean $\pm$ SD)	26.8 $\pm$ 4.3	27.6 $\pm$ 3.6	25.4 $\pm$ 7.2
Nulliparity (n, %)	52 (45%)	34 (54%)	24 (71%)
Gravidity (median with range)	3 [1–9]	3 [1–8]	2 [1–6]
Parity (median with range)	2 [1–8]	2 [1–7]	2 [1–6]
Pregnancy BMI at serum sampling (kg/m ²) (median with range)	25.1 [19.2–31]	26.4 [20.4–31.2]	24.9 [20.8–30.4]
<25 (n, %)	76 (66%)	21 (33%)	20 (59%)
$\geq$ 25 (n, %)	39 (34%)	42 (67%)	14 (41%)
Systolic BP (mm Hg) (mean $\pm$ SD)	108 $\pm$ 12*	148 $\pm$ 16**	162 $\pm$ 14***
Diastolic BP (mm Hg) (mean $\pm$ SD)	68 $\pm$ 9.6*	96 $\pm$ 6.2**	114 $\pm$ 7.2***
MAP (mm Hg) (median with range)	81.2* [69–93.4]	114.2** [104.8–128.9]	133.1*** [115.4–176]
Gestational age at serum sampling (wk) (median with range)	33 [24–40]	33 [24–37]	31 [24–35]
Gestational age at delivery (wk) (median with range)	38 [35–40]	35 [30–39]	31 [25–35]
Fetal birthweight (gr) (mean $\pm$ SD)	3412 $\pm$ 456*	2628 $\pm$ 758**	2035 $\pm$ 1124***
Growth-restricted baby (n, %)	1 (1%)*	9 (14%)**	25 (73.5%)*
hs-CRP (mg/L) (mean $\pm$ SD)	5.8 $\pm$ 4.2	9.6 $\pm$ 7.1**	23.4 $\pm$ 16.5***

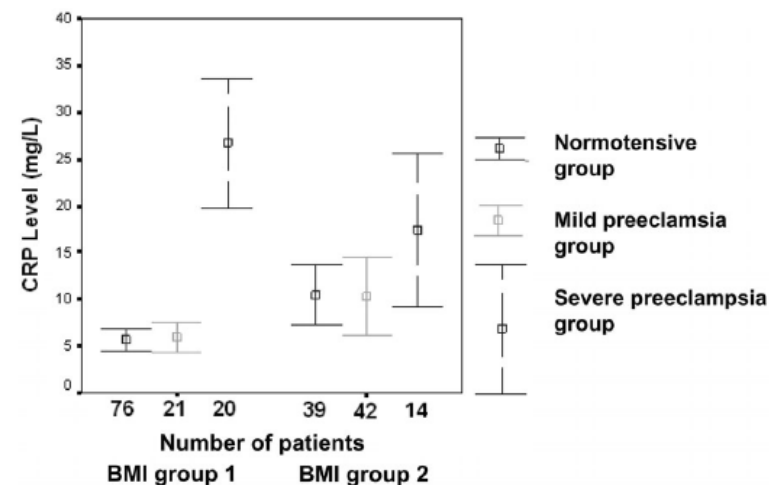
doi:10.1111/j.1447-0756.2010.01279.x

J. Obstet. Gynaecol. Res. Vol. 36, No. 5: 970–977, October 2010

Association of maternal serum high sensitive C-reactive protein level with body mass index and severity of pre-eclampsia at third trimester

Ibrahim E. Ertas¹, Serkan Kahyaoglu¹, Bulent Yilmaz¹, Murat Ozel¹, Necdet Sut², Melih A. Guven² and Nuri Danisman¹

¹Department of High Risk Pregnancy, Zekai Tahir Burak Women's Health Education and Research Hospital, ²Anatolia Advanced Level Ultrasonography Center, Ankara, and ²Department of Biostatistics, Trakya University Faculty of Medicine, Edirne, Turkey



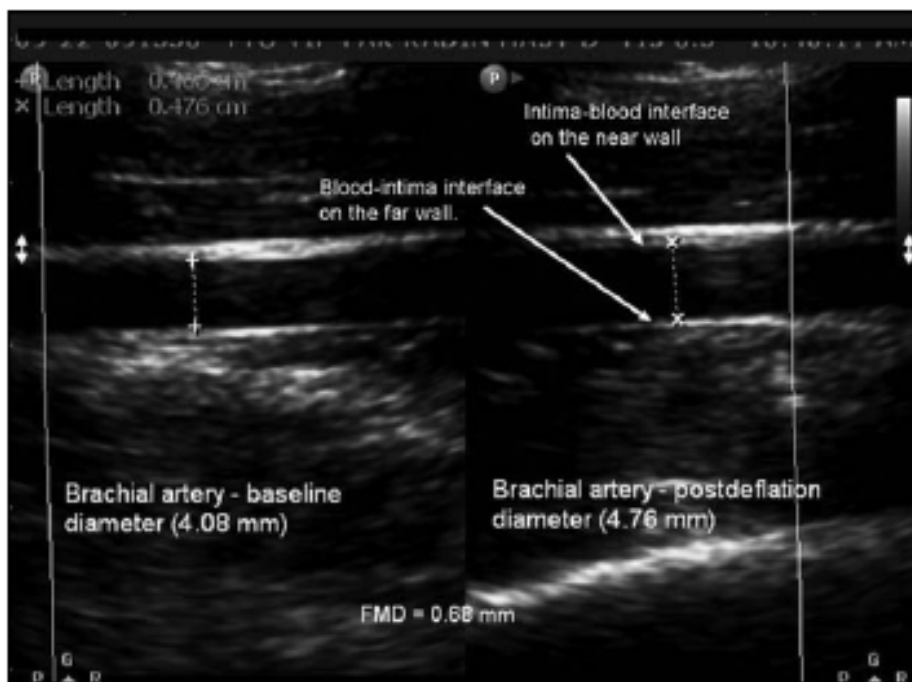


FIGURE 3. Ultrasound image of the brachial artery. Baseline diameter and postdeflation diameter.

The Relationship Between Brachial Artery Flow-Mediated Dilatation, High Sensitivity C-Reactive Protein, and Uterine Artery Doppler Velocimetry in Women with Pre-Eclampsia

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JOURNAL OF CLINICAL ULTRASOUND

VOL. 39, NO. 4, MAY 2011

TABLE 2
Plasma Fibrinogen, Serum High Sensitivity C-Reactive Protein Levels, FMD, FMD %, and Abnormal Doppler Velocimetry in Pre-Eclamptic and Normotensive Pregnant Women

	Pre-eclampsia (n = 35)	Normotensive (n = 35)	<i>p</i> value*
High sensitivity C-reactive protein (mg/L)	23 ± 4	5 ± 1	<0.01
FMD (mm)	0.3 ± 0.1	0.6 ± 0.1	<0.01
FMD %	8	15	<0.01
Abnormal UA-Doppler velocimetry, n (%)	11 (31)	0	<0.01

Data presented as mean ± SE or percentage (proportion).

Abbreviations: FMD, flow-mediated dilatation; UA, uterine artery; NS, not statistically significant (*p* > 0.05).

* *p* values are for one-way analysis of variance (ANOVA) and Z-test.

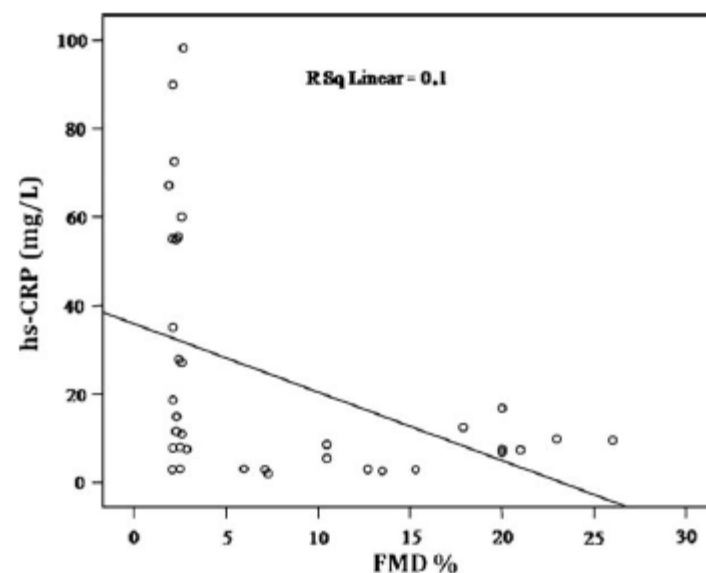


FIGURE 5. Correlation of flow-mediated dilatation percentage (FMD%) and serum high sensitivity C-reactive protein (hs-CRP) levels in women with pre-eclampsia (Pearson's correlation coefficient *r* = -0.436; *p* < 0.01).

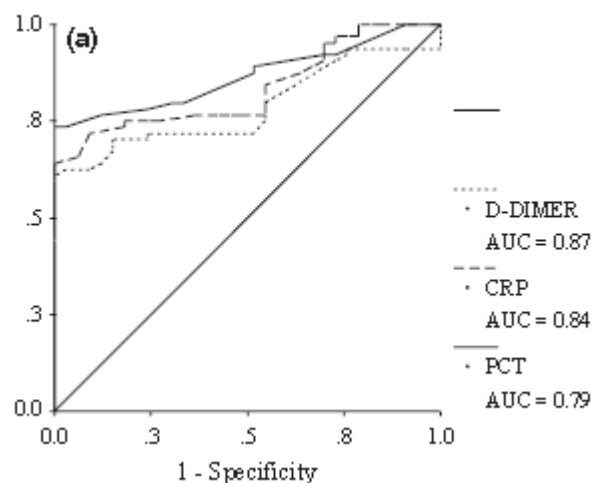


Table I Demographic Characteristics of the Study and Control Groups

	Control (n 33) Mean $\pm$ S.D. Median (min max)	Pre-eclampsia (n 64) Mean $\pm$ S.D. Median (min max)	P
Age(year)	29.7 $\pm$ 5.8 30 (20 44)	28.9 $\pm$ 7.5 28 (16 56)	0.599
BMI	31.9 $\pm$ 4.2 32.4 (24 40)	30.4 $\pm$ 4.8 30.0 (23 46)	0.133
GA(week)	35.1 $\pm$ 2.6 35 (30 39)	35.5 $\pm$ 4.1 37 (27 41)	0.656
MAP(mmHg)	91.5 $\pm$ 9.6 90.0 (75 105)	128.9 $\pm$ 20.6 127.5 (90 183)	0.001
SBP(mmHg)	111.5 $\pm$ 13.3 110 (90 130)	155.6 $\pm$ 27.0 150 (140 230)	0.001
DBP(mmHg)	71.5 $\pm$ 6.7 70 (60 80)	99.3 $\pm$ 14.8 100 (90 160)	0.001

BMI, Body Mass Index; GA, Gestational age; MAP, Mean arterial blood pressure; SBP, Systolic blood pressure; DBP, Diastolic blood pressure.

Table V Results of Logistic Regression Analysis

	OR	95% CI	P
Age	1.02	0.92 1.14	0.650
BMI > 31	1.69	0.36 7.89	0.503
GA < 34	1.87	0.44 7.96	0.395
PCT > 0.065ng/mL	15.68	3.15 78.10	0.001
CRP > 0.45 mg/dL	14.29	3.08 66.34	0.001
D-DIMER > 1.42 mg/L	4.97	1.22 20.29	0.026

OR, Odds ratio; CI, Confidence interval.

Gulec UK, Ozgunen FT, Guzel AB, Buyukkurt S, Seydaoglu G, Urunsak IF, Evruke IC.

An analysis of C-reactive protein, procalcitonin, and D-Dimer in pre-eclamptic patients. Am J Reprod Immunol 2012

C-reactive protein levels, blood pressure and the risks of gestational hypertensive complications: The Generation R Study

Layla L. de Jonge^{a,b,c}, Eric A.P. Steegers^d, Gesina D.S. Ernst^{a,b,c}, Jan Lindemans^e, Henk Russcher^e, Albert Hofman^b and Vincent W.V. Jaddoe^{a,b,c}

			Preeclampsia
<5.0 mg/l	3001	53	Reference
5.0–9.9 mg/l	1485	27	1.03 (0.65–1.64)
10.0–14.9 mg/l	526	14	1.52 (0.84–2.76)
15.0–19.9 mg/l	188	7	2.15 (0.96–4.80)
≥20.0 mg/l	229	5	1.24 (0.49–3.14)

Conclusion Our results suggest that first-trimester C-reactive protein levels are associated with SBP and DBP levels throughout pregnancy and with gestational hypertensive complications, but these associations are largely explained by maternal BMI. *J Hypertens* 29:2413–2421 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.

DOES C-REACTIVE PROTEIN PREDICT RECURRENT PREECLAMPSIA?

Hilary S. Gamill, M.D.^a, Robert W. Powers, Ph.D.^a, Rebecca G. Clifton, Ph.D.^b, J. Peter Van Dorsten, M.D.^c, John C. Hauth, M.D.^d, Mark A. Klebanoff, M.D.^e, Marshall D. Lindheimer, M.D.^f, Baha Sibai, M.D.^g, Mark Landon, M.D.^h, Menachem Miodovnik, M.D.ⁱ, and Mitchell Dombrowski, M.D.^j for the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network, Bethesda, MD

Abstract

Objective—Evaluate association of the inflammatory marker C-reactive protein with recurrent preeclampsia.

Methods—Serum samples collected longitudinally in women with previous preeclampsia from the Maternal-Fetal Medicine Units Network trial of aspirin to prevent preeclampsia were assayed for CRP.

Results—Of 255 women studied, 50 developed recurrence. Baseline C-reactive protein concentration was similar between women who did and did not recur. After adjusting for confounders, neither elevated baseline C-reactive protein nor its change over gestation was associated with recurrence.

Conclusion—In this group of women with previous preeclampsia, neither baseline C-reactive protein concentration nor change in concentration over gestation was associated with recurrent preeclampsia.

Table 2

Baseline CRP concentration and change in CRP are not associated with recurrence of preeclampsia

	Preeclampsia (n=50)	Controls (n=205)		
	Median (range)	Median (range)	OR (95% CI) ##	Adjusted OR (95% CI) ##
Baseline CRP (mg/dL)	1.17 (0.09, 5.72)	1.01 (0.01, 4.97)	1.000 (1.000, 1.000)	1.0 (1.000, 1.000) *
CRP closest to delivery (mg/dL)	0.71 (0.06, 2.94)	0.76 (0.01, 4.62)		
Change in CRP (mg/dL)	−0.02 (−0.22, 0.30)	−0.02 (−0.43, 0.05)	0.996 (0.992, 1.001)	0.993 (0.986, 1.000) #

Thrombopénie

- Anomalie d' hémostasie la plus fréquente
- Critère de gravité?
(15% des PE, 50% ds formes graves)
- Pathogénie mixte : consommation, MAT, immuno
- Conséquence : macrocytose

Annales Françaises d'Anesthésie et de Réanimation 29 (2010) e121–e134



Disponible en ligne sur
 ScienceDirect
www.sciencedirect.com

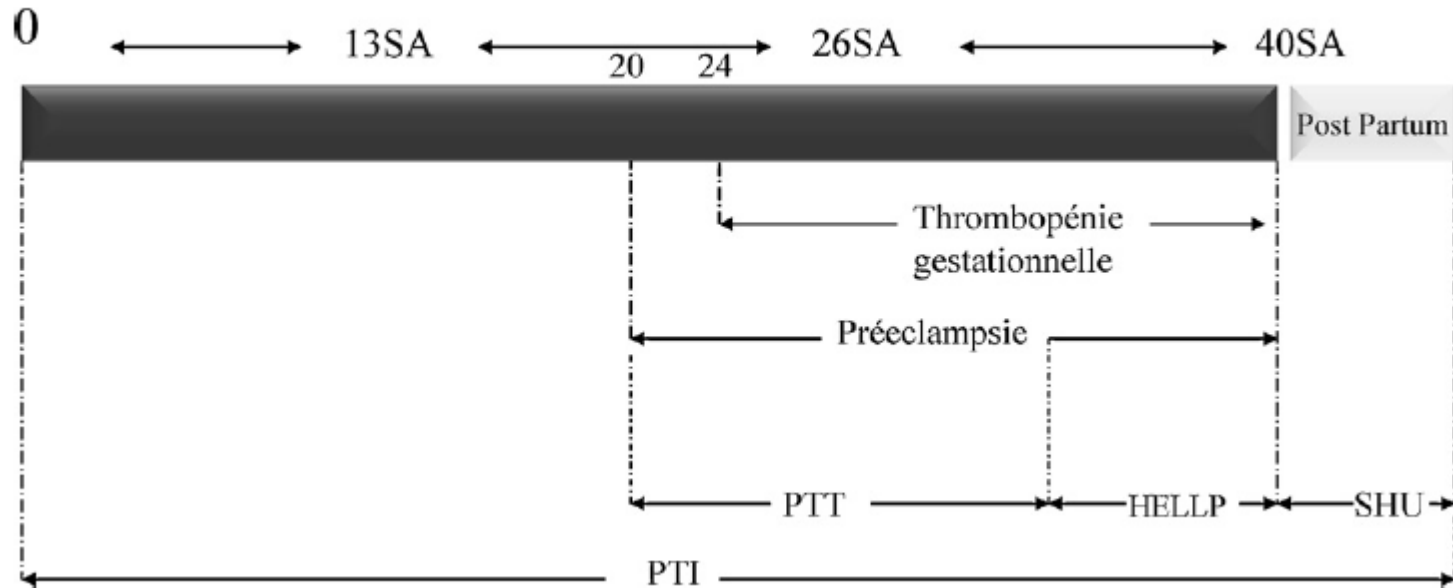
Elsevier Masson France
EM|consulte
www.em-consulte.com

Recommandations formalisées d'experts

Hémostasie et prééclampsie[☆]

Clotting disorders and preeclampsia

A.-S. Ducloy-Bouthors



Toutes les thrombopénies de la grossesse ne sont pas des pré éclampsies.....

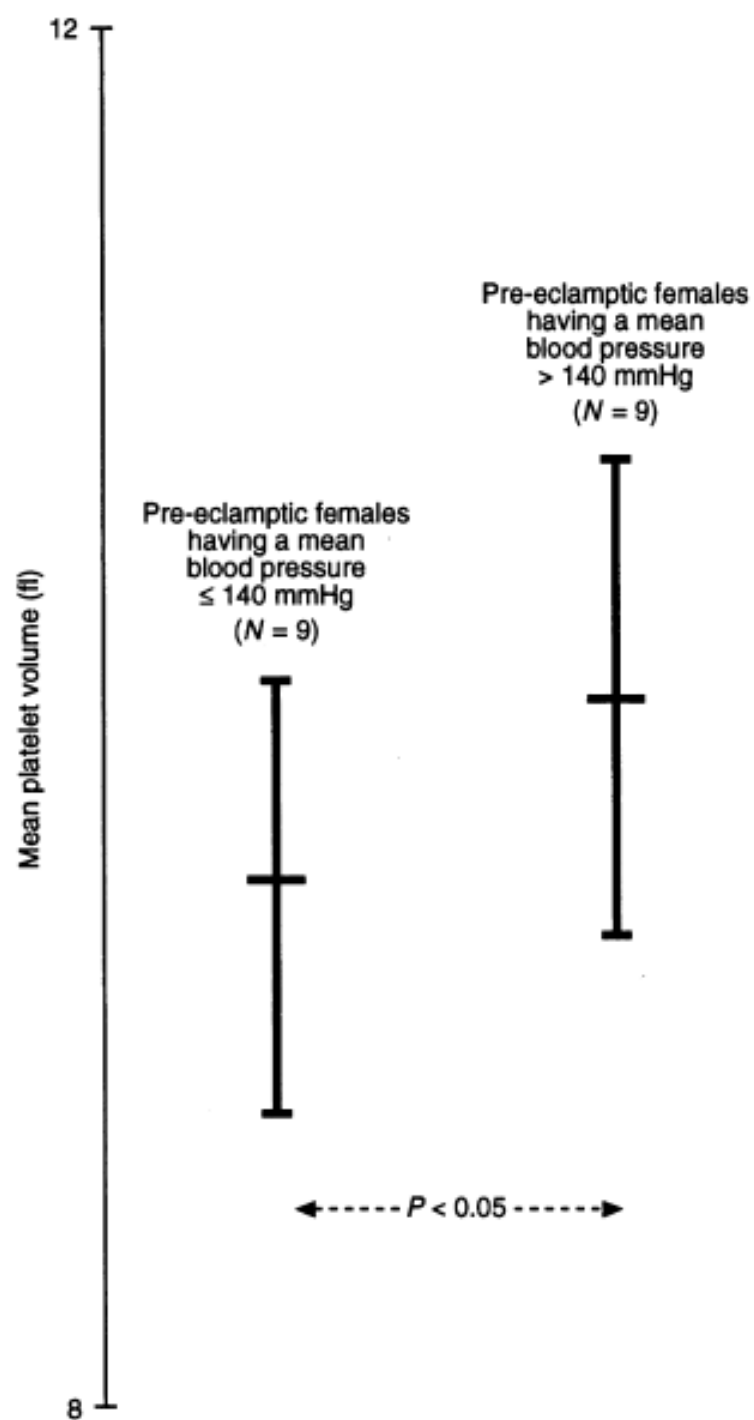
	Pré éclampsie	Normale	
	N = 15	N = 11	
Plaquettes (G/L)	216 $\pm$ 45	264 $\pm$ 113	NS
Vol. plaq (fl)	9,8 $\pm$ 0,7	8,8 $\pm$ 1,2	p<0,01

European Journal of Clinical Investigation (2000) **30**, 1113–1118

The use of platelet density and volume measurements to estimate the severity of pre-eclampsia

P. Järemo, T. L. Lindahl, C. Lennmarken and H. Forsgren

Värmevårdskliniken, Norrköping, Sweden



Volume plaquettaire et sévérité de la pré éclampsie

European Journal of Clinical Investigation (2000) **30**, 1113-1118

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Table 5

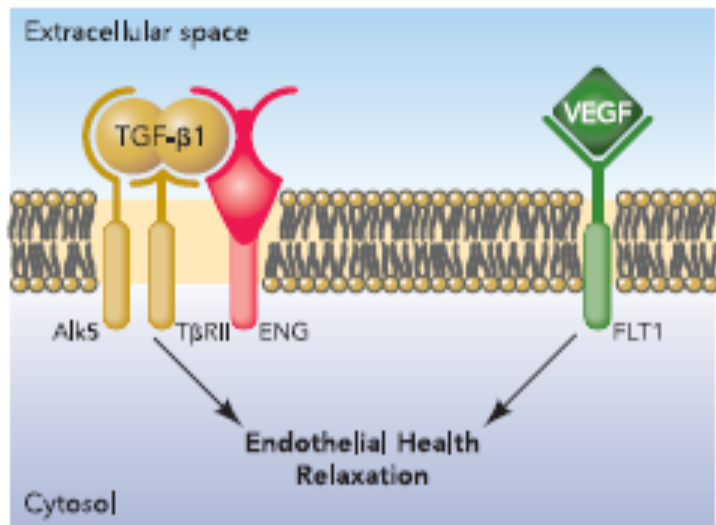
Post-partum complications in women with preeclampsia and/or HELLP syndrome according to biological features

	n = 453	Women with post-partum complications		
		n (%) ²	OR	IC 95%
Platelet count $<100 \times 10^6/\text{mm}^3$	200 (44.2)	50 (25)	2.08	1.25–3.47
Hemolysis	194 (42.8)	49 (25.3)	2.09	1.26–3.47
Haptoglobin ($<0.4 \text{ g/l}$)	174 (38.4)	43 (24.7)	1.85	1.12–3.06
LDH ($>600 \text{ UI/l}$)	92 (20.3)	32 (37.6)	3.10	1.79–5.37
Peripheral blood smear	102 (22.5)	30 (35.3)	2.24	1.30–3.87
Antenatal fibrinogen $<2 \text{ g/l}$	62 (13.7)	6 (9.7)	0.42	0.16–1.08
Presence of FDP	51 (11.3)	16 (31.4)	2.21	1.10–4.39
D-Dimer $>2000 \text{ ng/ml}$	192 (42.4)	45 (23.4)	1.69	1.03–2.79
Serum uric acid $>360 \mu\text{mol/l}$	312 (68.9)	72 (23.1)	2.95	1.51–5.87
Serum creatinine $>120 \mu\text{mol/l}$	29 (6.4)	12 (41.4)	3.39	1.44–7.94
Aspartate-aminotransferase $>75 \text{ UI/l}$	158 (34.9)	34 (21.5)	1.31	0.78–2.20
Proteinuria $>5 \text{ g/l}$	150 (33.1)	42 (28.0)	2.35	1.41–3.91

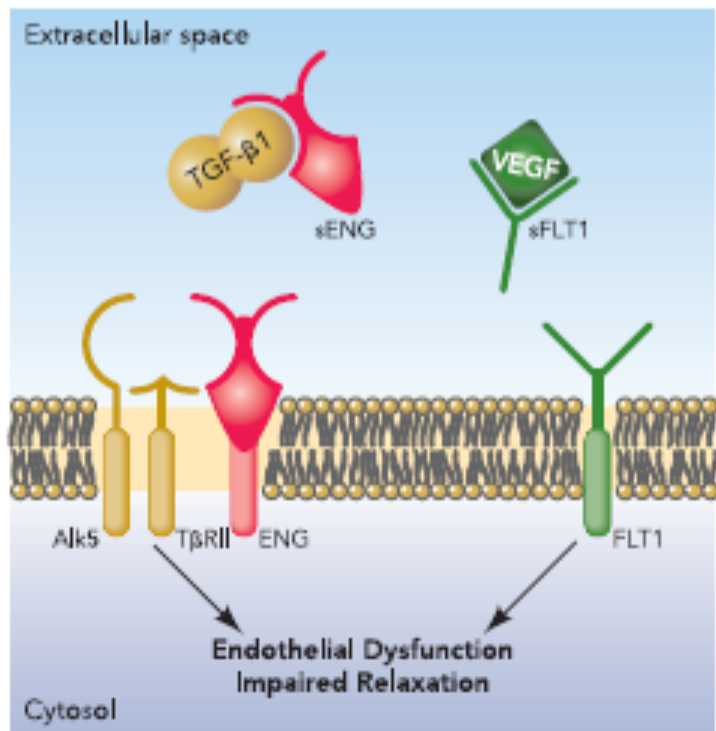
Values are reported as means $\pm$ S.D. or n (%); LDH: lactate dehydrogenase; FDP: fibrin degradation products.² Number of events for patients with post-partum complication/total number of events.

Les marqueurs en développement

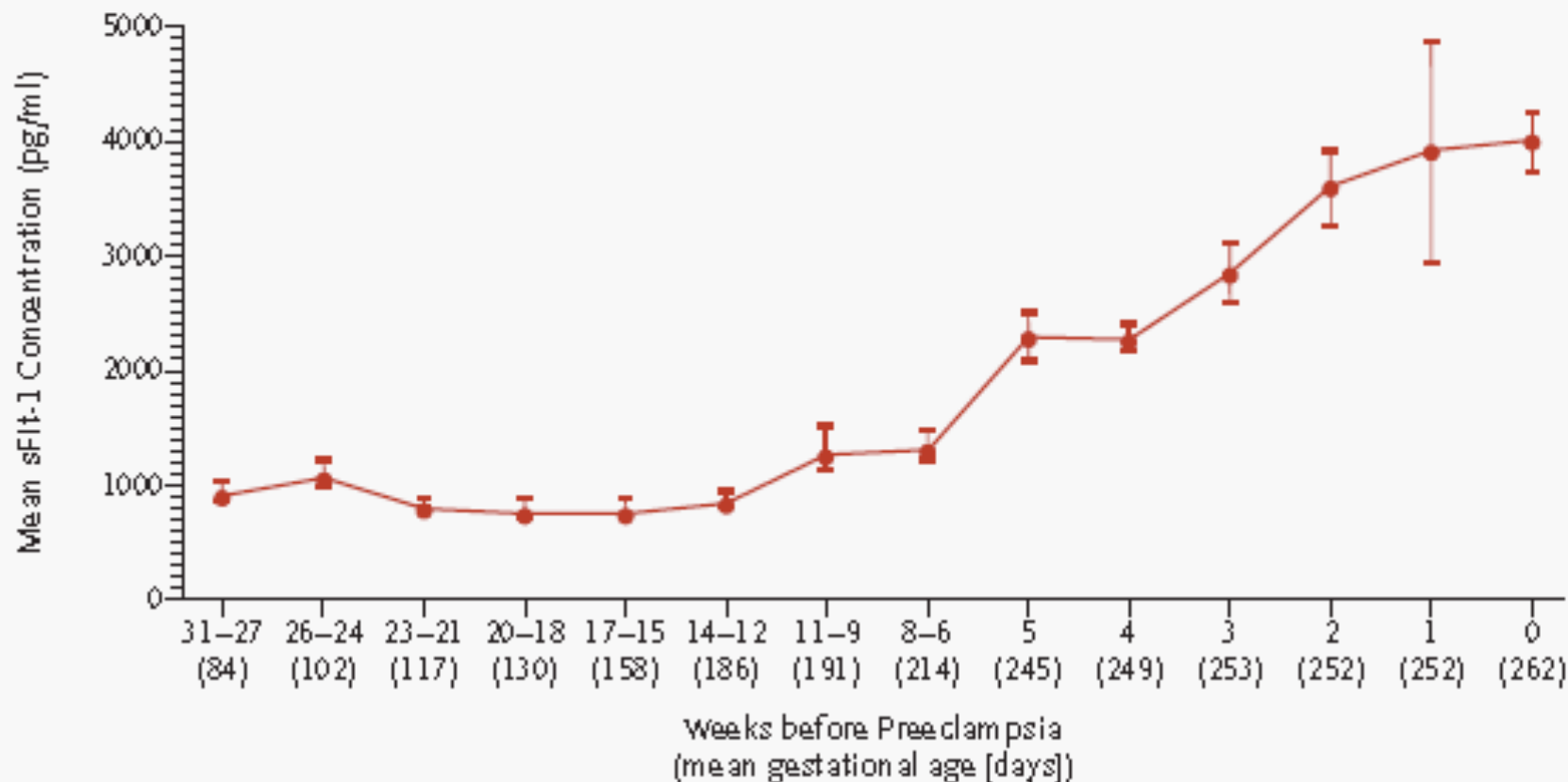
Normal



Preeclampsia



Les marqueurs de
l'angiopathie



No. of specimens

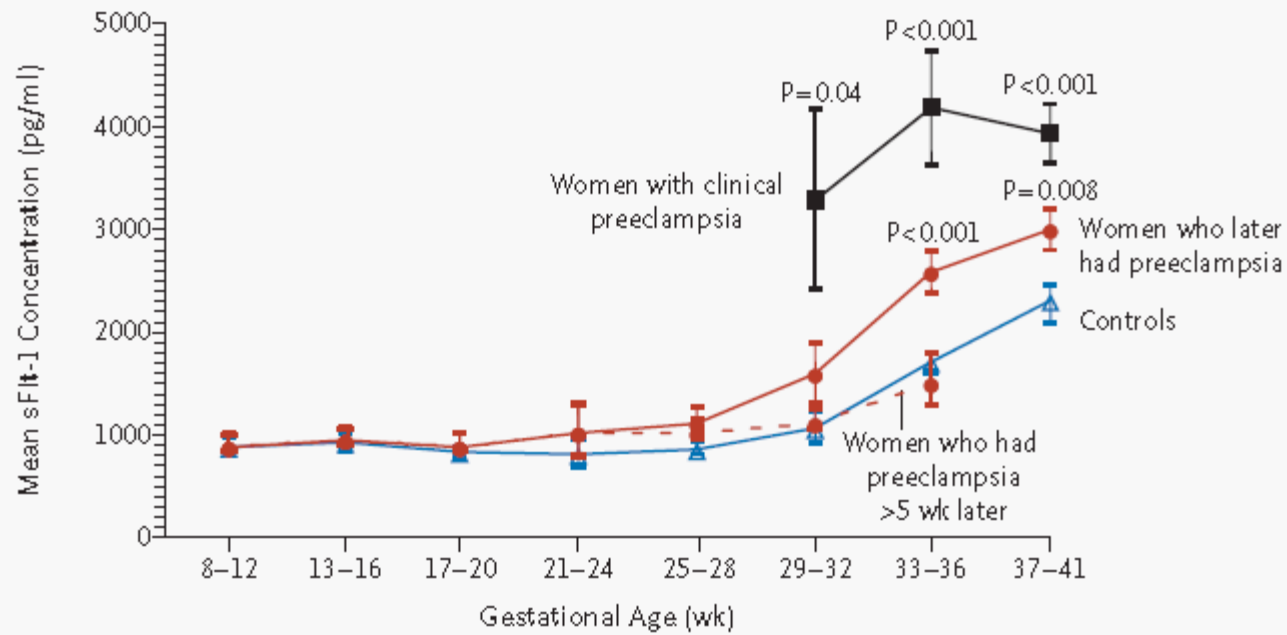
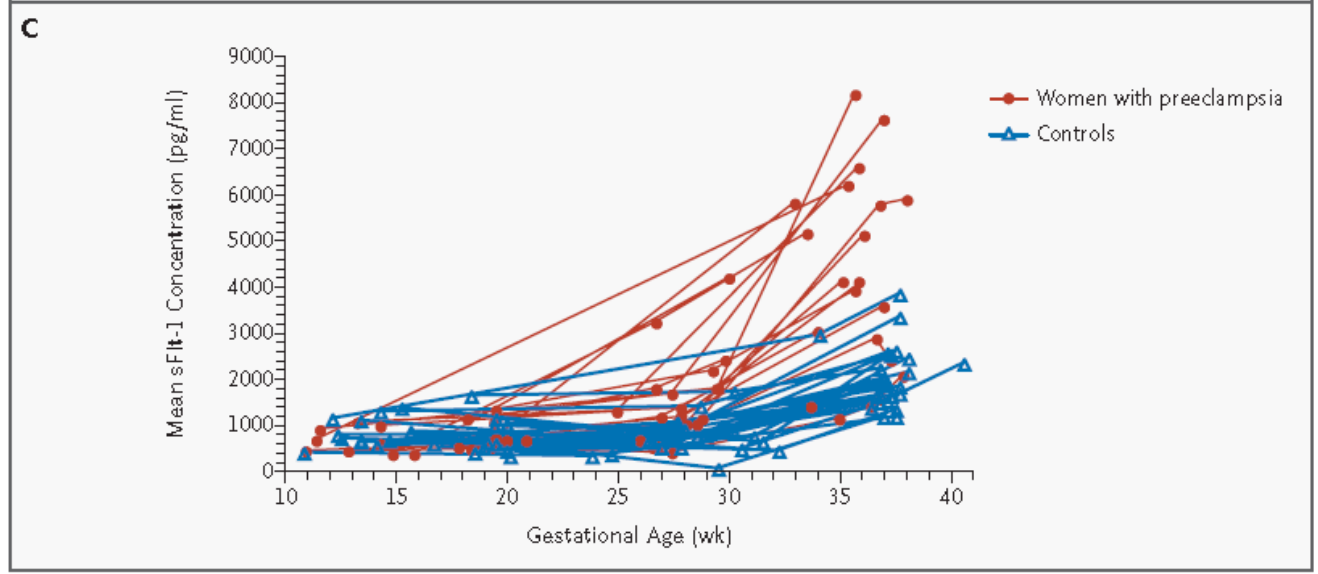
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The NEW ENGLAND JOURNAL of MEDICINE

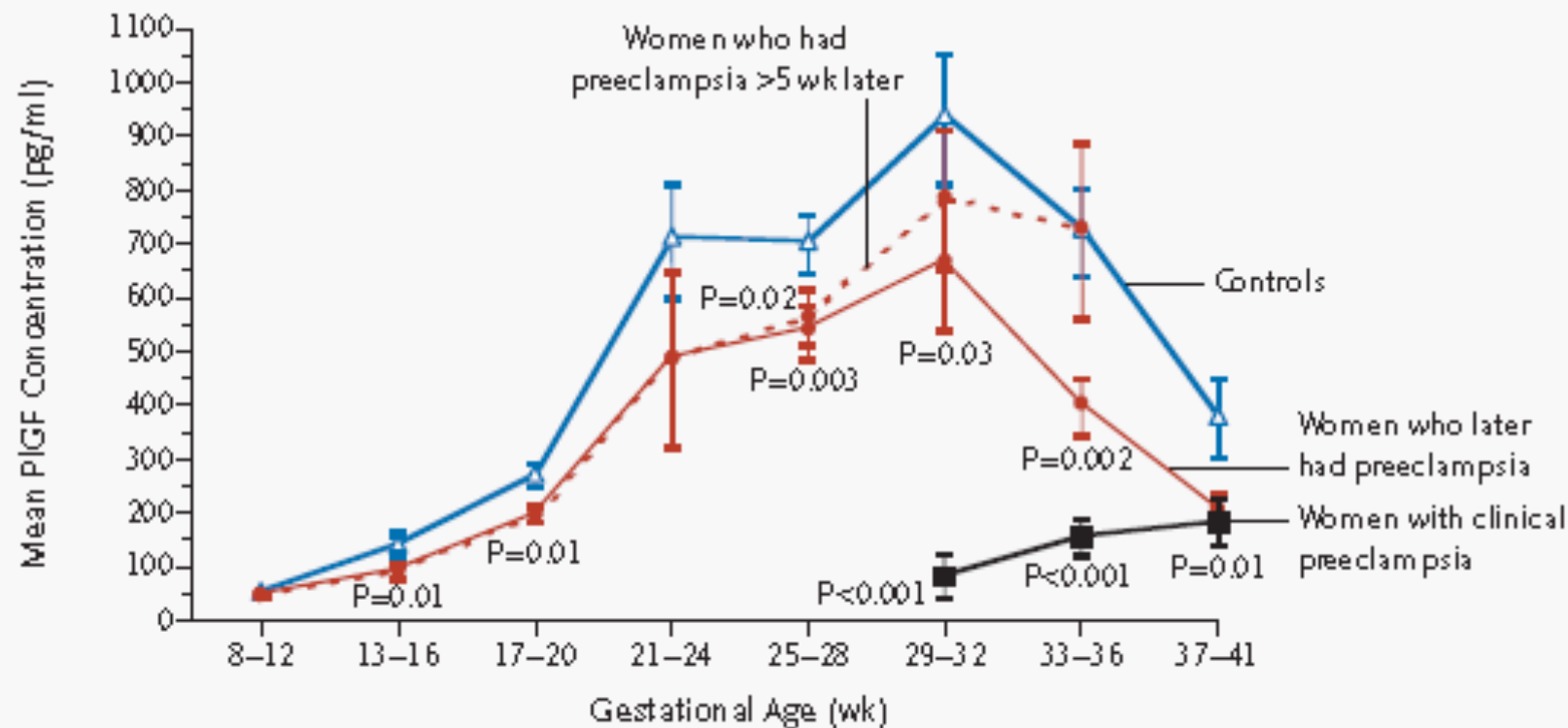
ORIGINAL ARTICLE

Circulating Angiogenic Factors and the Risk of Preeclampsia

Richard J. Levine, M.D., M.P.H., Sharon E. Maynard, M.D., Cong Qian, M.S.,
Kee-Hak Lim, M.D., Lucinda J. England, M.D., M.S.P.H., Kai F. Yu, Ph.D.,
Enrique F. Schisterman, Ph.D., Ravi Thadhani, M.D., M.P.H.,
Benjamin P. Sachs, M.B., B.S., D.P.H., Franklin H. Epstein, M.D.,
Baha M. Sibai, M.D., Vikas P. Sukhatme, M.D., Ph.D.,
and S. Ananth Karumanchi, M.D.



A



No. of specimens

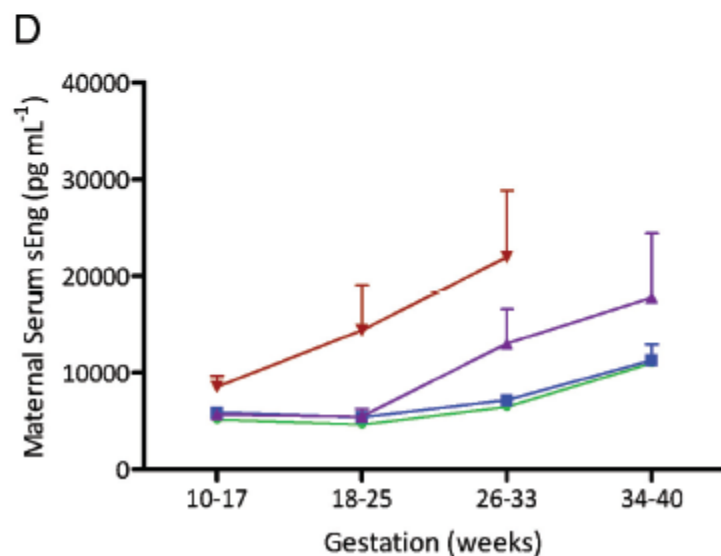
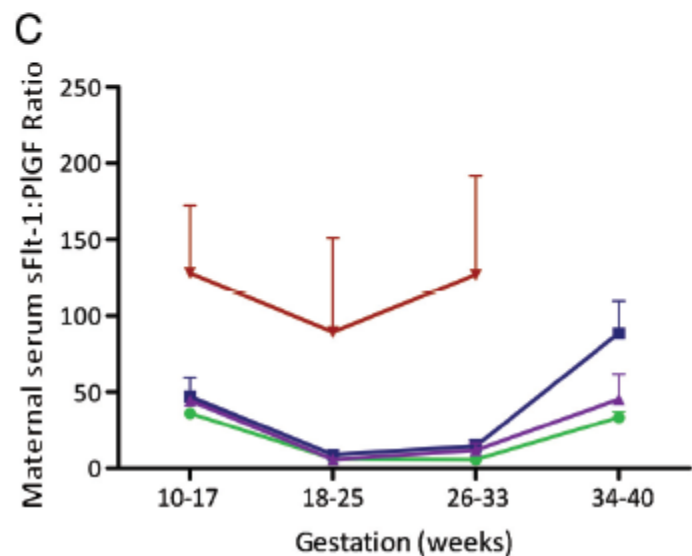
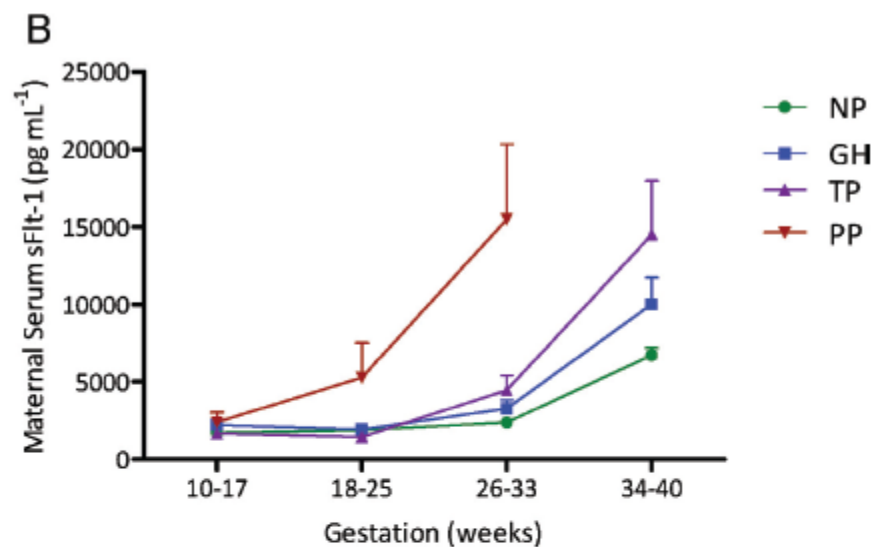
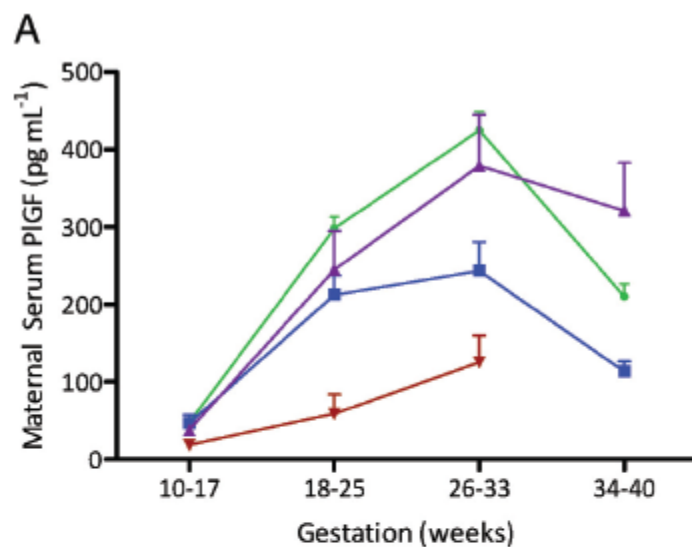
Controls	20	44	56	9	72	21	70	21
Before preeclampsia	21	43	56	6	75	23	57	19
>5 wk before preeclampsia	21	43	56	6	71	19	8	—
During preeclampsia	—	—	—	—	—	2	14	26

THE NEW ENGLAND JOURNAL of MEDICINE

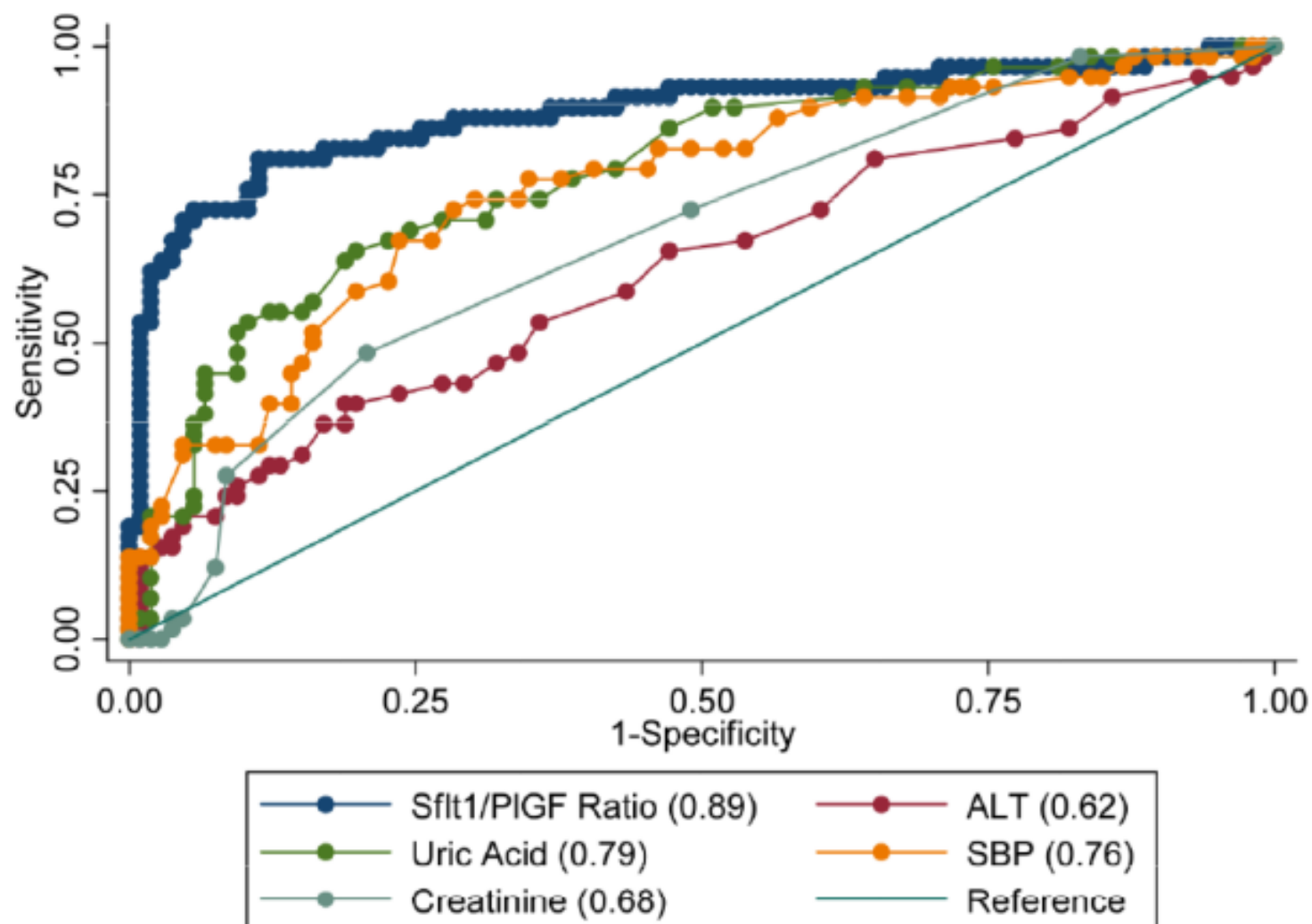
ORIGINAL ARTICLE

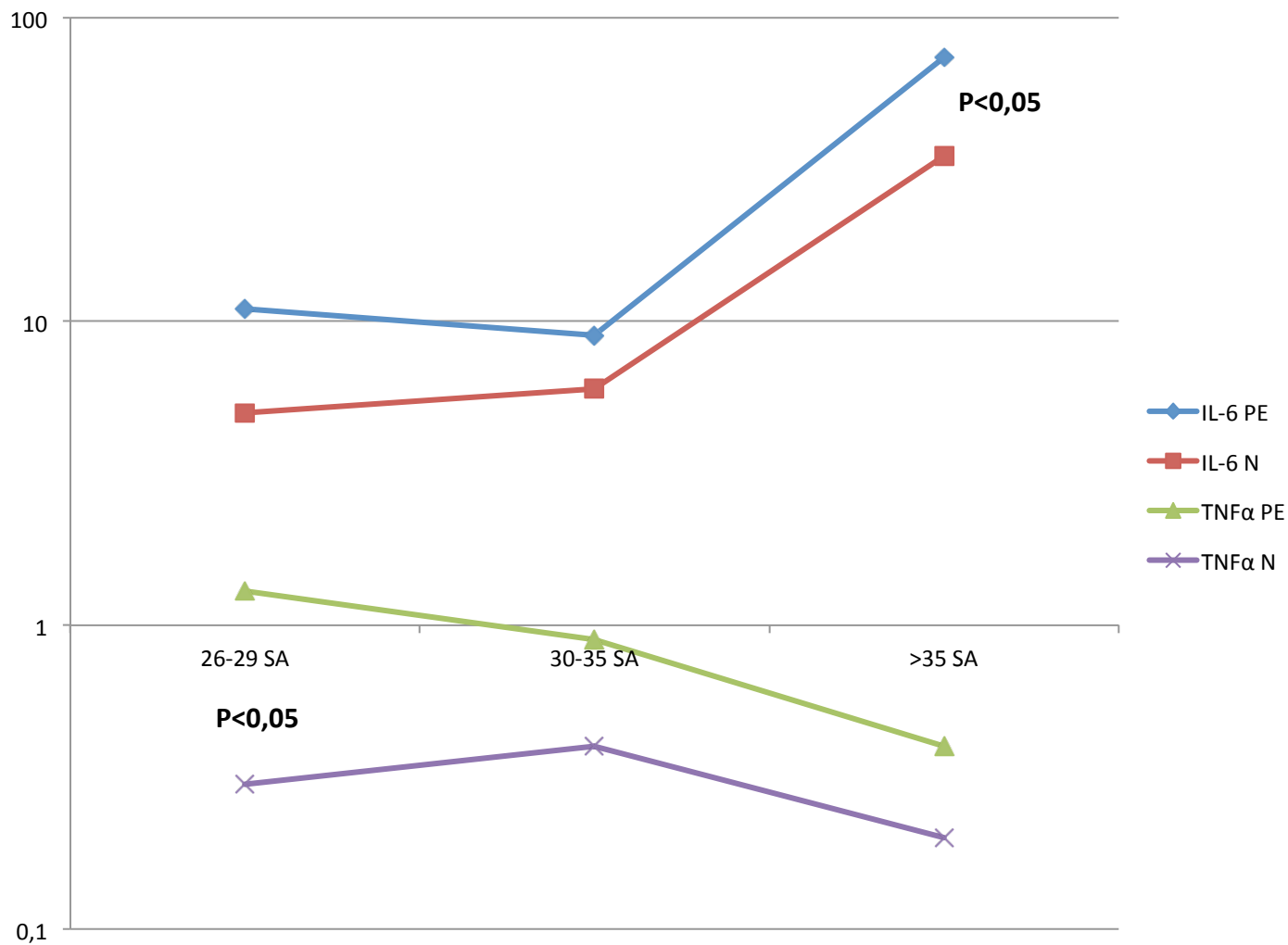
Circulating Angiogenic Factors and the Risk of Preeclampsia

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Baha M. Sibai, M.D., Vikas P. Sukhatme, M.D., Ph.D.,
and S. Ananth Karumanchi, M.D.



(*Circulation*. 2010;122:478-487.)





AOGS

ACTA Obstetrica et Gynecologica



Scandinavica

MAIN RESEARCH ARTICLE

Longitudinal measurement of cytokines in pre-eclamptic and normotensive pregnancies

CAMILLA S. KRONBORG¹, JAKOB GJEDSTED², ERIK VITTINGHUS³, TROELS K. HANSEN^{2,4}, JIM ALLEN¹ & ULLA B. KNUDSEN¹

Table 2. Descriptive Analysis for ADAMTS13, VWF, P-sel, TSP-1, IL-6, and CRP Plasma Levels in PE Cases and in Controls

Laboratory Data	Cases		Controls		P
	n	Mean±SD (Median; Q1; Q3)	n	Mean±SD (Median; Q1; Q3)	
ADAMTS13 activity, %	140	66±17 (64; 53; 79)	138	78±16 (77; 67; 87)	<0.0001
ADAMTS13 Ag, ng/mL	139	559±183 (543; 418; 700)	140	680±172 (652; 566; 759)	<0.0001
ADAMTS13 activity/Ad	139	0.125±0.032 (0.121; 0.104; 0.146)	137	0.119±0.031 (0.115; 0.097; 0.135)	0.16
VWF:Ag, IU/mL	140	363±128 (350; 263; 449)	140	221±88 (214; 149; 269)	<0.0001
P-sel, ng/mL	139	52±29 (44; 32; 66)	138	35±17 (32; 21; 47)	<0.0001
TSP-1, ng/mL	130	787±760 (459; 293; 1025)	131	713±494 (596; 333; 1017)	0.69
IL-6, pg/ml	138	4.97±8.57 (2.34; 0.96; 4.39)	137	1.22±1.20 (0.88; 0.62; 1.24)	<0.0001
CRP, ng/mL	130	10.7±13.1 (5.1; 1.9; 12.6)	127	4.1±3.9 (2.9; 1.7; 5.3)	<0.0001
Platelet count, Giga/L	140	197±80.7 (189; 141.5; 232.5)		NA	...

P was determined by signed rank test. Q1 indicates lower quartile; Q3, upper quartile; ADAMTS13 activity/Ag, ADAMTS13 specific activity; NA, not available.

Von Willebrand Factor and ADAMTS13 A Candidate Couple for Preeclampsia Pathophysiology

Alain Stepanian, Marie Cohen-Moatti, Thibaut Sanglier, Paulette Legendre, Nejma Ameziane,
Vassilis Tsatsaris, Laurent Mandelbrot, Dominique de Prost, Agnès Veyradier, for the ECLAXIR
study group

(*Arterioscler Thromb Vasc Biol.* 2011;31:1703-1709.)

Indicateurs mixtes : Biomarqueurs + Doppler

TABLE 6
Sensitivity and positive likelihood ratio of different combinations of maternal characteristics, PIGF, PAPP-A, Inhibin-A, and uterine artery Doppler at 11-13 weeks' gestation, for a fixed 10% false-positive rate

Variable	Preeclampsia			Severe preeclampsia			Early-onset preeclampsia		
	Sensitivity	LR ⁺	LR ⁻	Sensitivity	LR ⁺	LR ⁻	Sensitivity	LR ⁺	LR ⁻
Maternal characteristics alone	30.0	3.0	0.78	45.5	4.5	0.60	55.6	5.6	0.49
Maternal characteristics plus:									
L-PI	35.1	3.5	0.72	42.1	4.2	0.64	50.0	5.0	0.55
PIGF	40.9	4.1	0.66	61.5	6.1	0.43	75.0	7.5	0.28
PAPP-A	32.5	3.2	0.75	54.5	5.4	0.50	55.6	5.6	0.49
Inhibin-A	35.0	3.5	0.72	50.0	5.0	0.55	55.6	5.6	0.49
PIGF, PAPP-A	40.9	4.1	0.66	53.8	5.4	0.51	75.0	7.5	0.28
PIGF, Inhibin-A	40.9	4.1	0.66	53.8	5.4	0.51	75.0	7.5	0.28
PAPP-A, Inhibin-A	32.5	3.2	0.75	54.5	5.5	0.50	55.6	5.6	0.49
PIGF, Inhibin-A, PAPP-A	31.8	3.2	0.76	53.8	5.4	0.51	75.0	7.5	0.28
Inhibin, PAPP-A, L-PI	32.4	3.2	0.75	52.6	5.3	0.53	37.5	3.7	0.69
PIGF, Inhibin-A, PAPP-A, L-PI	40.0	4.0	0.67	54.5	5.5	0.50	100.0	10.0	0.00

All models including PIGF are based on 531 women only, including 498 unaffected, 22 with preeclampsia (13 severe, 4 early-onset).

L-PI, lowest of uterine artery Doppler pulsatility indices; LR⁺, likelihood ratio for a positive test; PAPP-A, pregnancy-associated plasma protein-A; PIGF, placental growth factor.

Audibert. Screening for preeclampsia using first-trimester serum markers and uterine artery Doppler. *Am J Obstet Gynecol* 2010.

Et après l'accouchement.....

Table 2. Circulating Biomarkers in Women 5 to 8 Y Postpartum

Biomarkers	C (n=15)	PE (n=26)	P
hs-CRP, mg/L	0.64 (0.47 to 0.97)	1.23 (0.71 to 5.09)	0.02*
Calprotectin, $\mu\text{g/L}^\dagger$	572 (± 169)	730 (± 356)	0.06
sFIt-1, pg/mL ‡	70.9 (± 11.2)	79.7 (± 15.0)	0.05
sEng, ng/mL	4.33 (3.92 to 4.85)	4.12 (3.88 to 5.11)	0.9
VEGF, pg/mL	353 (227 to 559)	266 (125 to 458)	0.2
PlGF <15.6, pg/mL, % ‡	87	77	0.7
TAG, mmol/L	0.93 (0.75 to 1.31)	0.89 (0.67 to 1.49)	0.8
Tot chol, mmol/L ‡	5.18 (± 0.89)	5.31 (± 1.31)	0.8
HDL, mmol/L ‡	1.45 (± 0.32)	1.50 (± 0.38)	0.6
LDL, mmol/L	3.41 (1.89 to 4.52)	2.89 (1.62 to 7.23)	0.8

C indicates control; PE, preeclampsia; TAG, triglycerides; HDL, high-density

Table 3. Circulating Biomarkers in Children 5 to 8 Y Old

Biomarkers	C (n=14)	PE (n=19 to 20 §)	P
hs-CRP, mg/L	0.63 (0.27 to 0.93)	0.46 (0.23 to 0.91)	0.8
Calprotectin, $\mu\text{g/L}$	646 (490 to 950)	878 (454 to 1084)	0.5
sFIt-1, pg/mL ‡	92.1 (± 14.9)	93.6 (± 14.1)	0.8
sEng, ng/mL ‡	5.13 (± 0.72)	5.42 (± 0.83)	0.3
VEGF, pg/mL ‡	266 (± 146)	266 (± 191)	1.0
PlGF, pg/mL	18.4 (15.6 to 20.0)	16.5 (15.6 to 21.2)	0.8
PlGF <15.6, pg/mL, % ‡	40	48	0.3
TAG, mmol/L	0.58 (0.53 to 0.82)	0.60 (0.53 to 0.73)	0.9
Tot chol, mmol/L	4.43 (4.00 to 5.00)	5.01 (4.44 to 5.39)	0.04*
HDL, mmol/L ‡	1.41 (± 0.34)	1.60 (± 0.31)	0.1
LDL, mmol/L	1.53 (1.12 to 2.26)	1.81 (1.20 to 2.42)	0.3

C indicates control; PE, preeclampsia; TAG, triglycerides; HDL, high-density

Hypertension
JOURNAL OF THE AMERICAN HEART ASSOCIATION



Endothelial Function and Circulating Biomarkers Are Disturbed in Women and Children After Preeclampsia

Anne Stine Kvehaugen, Ralf Dechend, Heidi Bente Ramstad, Rebecca Troisi, Drude Fugelseth and Anne Cathrine Staff

Hypertension. 2011;58:63-69; originally published online May 23, 2011;

	Pre-eclampsia (n = 15)		Normal pregnancies (n = 11)	
	At delivery	3–12 months postpartum	At delivery	3–12 months postpartum
Platelet counts ($\times 10^9 \text{ L}^{-1}$)	216 ± 45	$316 \pm 45^{***}$	264 ± 113	$278 \pm 48^\dagger$
Mean platelet volume (fL)	9.8 ± 0.7	$9.2 \pm 0.6^{**}$	8.8 ± 1.2	$8.9 \pm 0.8^\dagger$
Soluble P-selectin (mg/L)	33 ± 16	$21 \pm 6^{**}$	31 ± 9	$24 \pm 7^*$

European Journal of Clinical Investigation (2000) **30**, 1113–1118

The use of platelet density and volume measurements to estimate the severity of pre-eclampsia

P. Järemo, T. L. Lindahl, C. Lennmarken and H. Forsgren
Värmehälsjukhuset, Norrköping, Sweden

Table 3. Postpartum (Median, 12 weeks; IQR, 6 to 32 Weeks) Maternal Serum Levels of Angiogenic and Antiangiogenic Factors in Subjects Who Had a Normotensive Pregnancy, Gestational Hypertension, Term Preeclampsia, or Preterm Preeclampsia

	Normotensive (n=79)		Gestational Hypertension (n=7)		Term Preeclampsia (n=10)		Preterm Preeclampsia (n=6)		P, ANOVA
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	
PlGF, pg/mL	8.1	0.17	10.77	0.06	11.99	1.59	11.56	0.61	0.005
sFlt-1, pg/mL	264.24	11.59	191.43	3.61	464.5	3.09	440.6	54.86	0.06
sFlt-1:PlGF ratio	27.67	1.34	17.74	0.80	38.73	0.65	38.11	3.16	0.29
sEng, pg/mL	4256	72	4819	109	3811	178	3990	136	0.53

Data are presented as geometric mean $\pm$ SEM and were compared by 1-way ANOVA.



**Prospective Study of Placental Angiogenic Factors and Maternal Vascular Function
Before and After Preeclampsia and Gestational Hypertension**
Muna Noori, Ann E. Donald, Aspasia Angelakopoulou, Aroon D. Hingorani and David J.
Williams

Circulation. 2010;122:478-487; originally published online July 19, 2010;

En pratique....

- Intérêts et limites du spot urinaire
- La CRPus : beaucoup d'incertitudes
- Les facteurs vasculaires : beaucoup d'espoir
- Le suivi du postpartum : beaucoup de questions

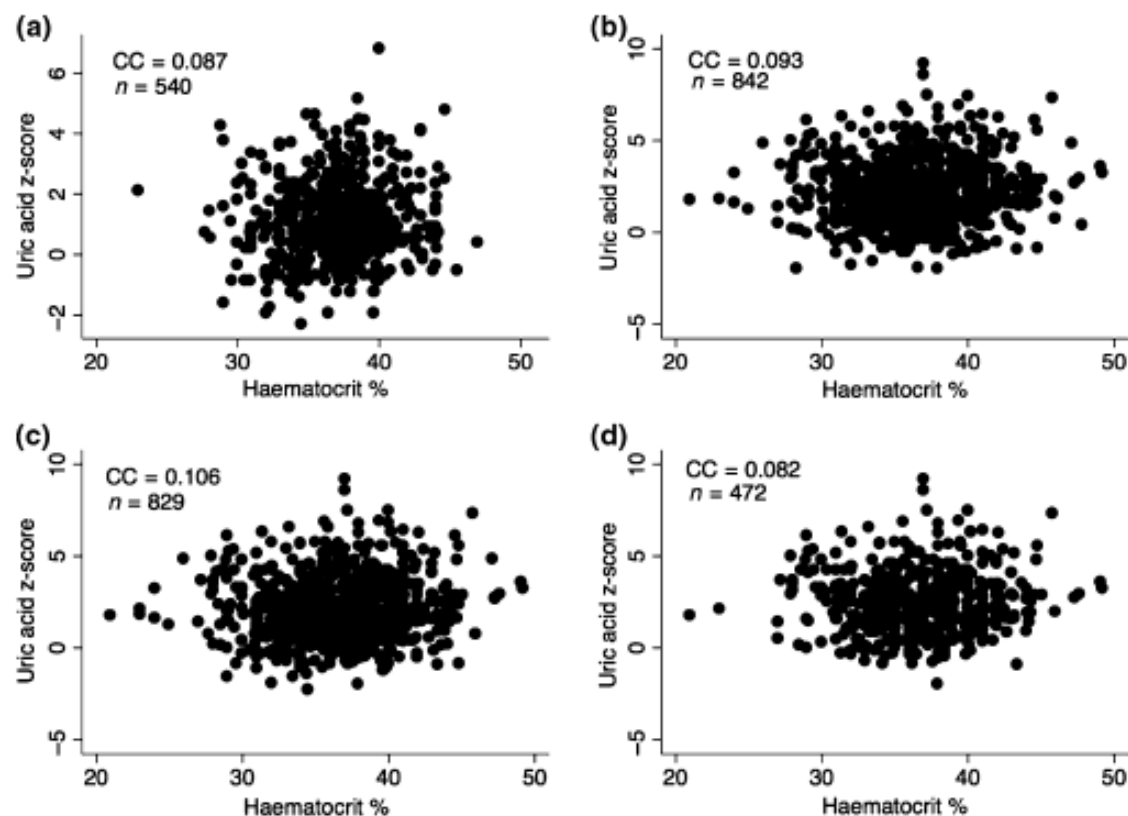
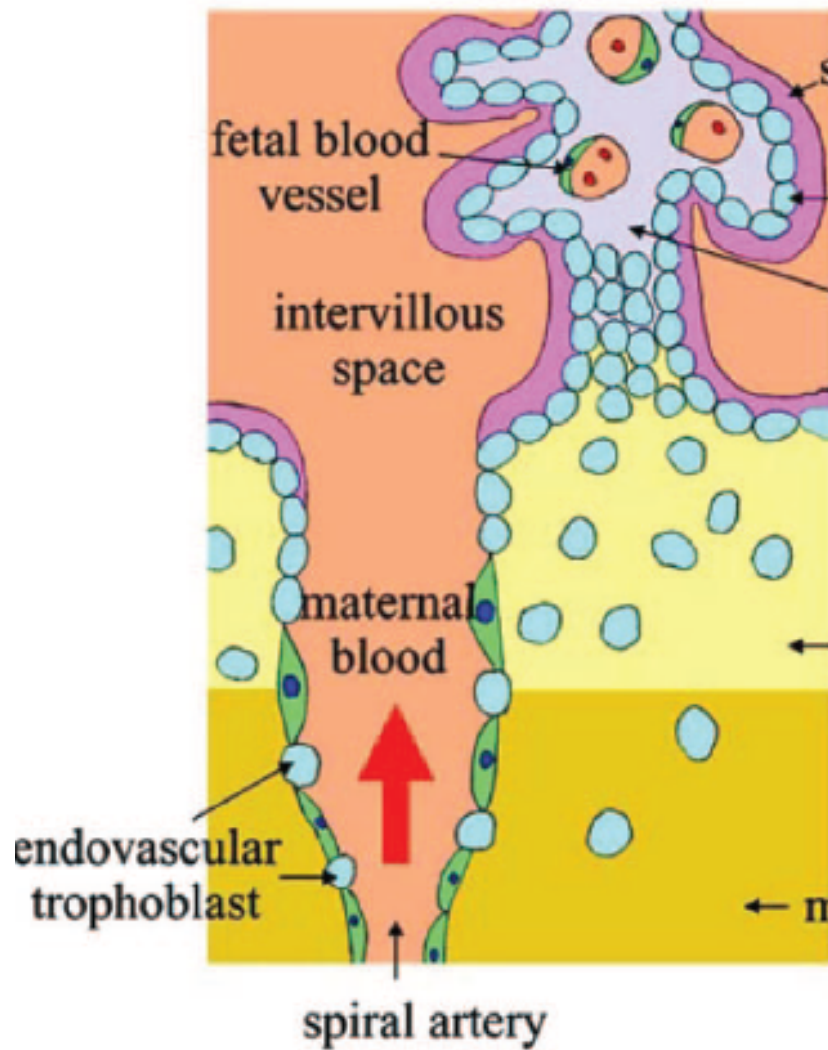


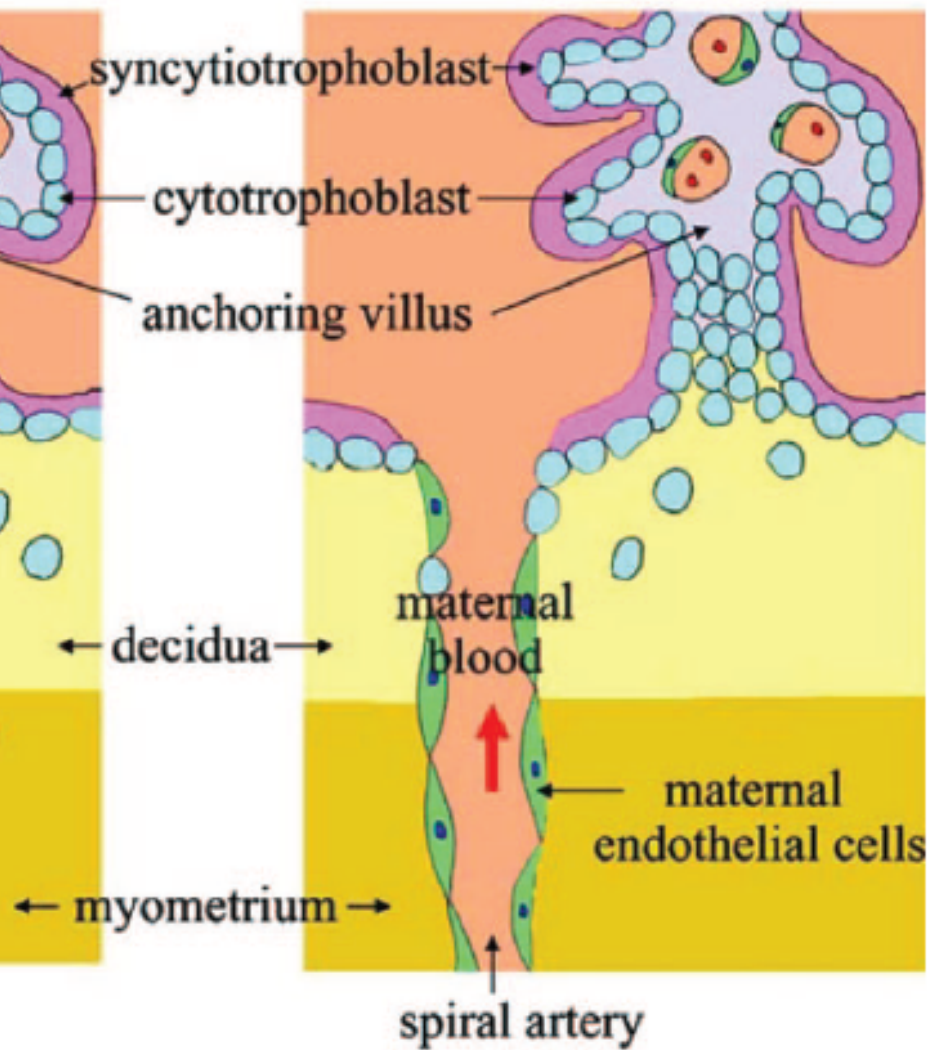
Figure 1. Scatterplots showing the lack of association between uric acid z-score (UA Z-s) and haematocrit by outcome; final diagnosis: gestational hypertension (a), final diagnosis: pre-eclampsia (b), composite adverse maternal outcome (c) and composite adverse fetal outcome (d). The Pearson product-moment correlation coefficient (CC) and sample size (n) for each association are shown.

Please cite this paper as: Hawkins T, Roberts J, Mangos G, Davis G, Roberts L, Brown M. Plasma uric acid remains a marker of poor outcome in hypertensive pregnancy: a retrospective cohort study. BJOG 2012;119:484–492.

normal



preeclampsia



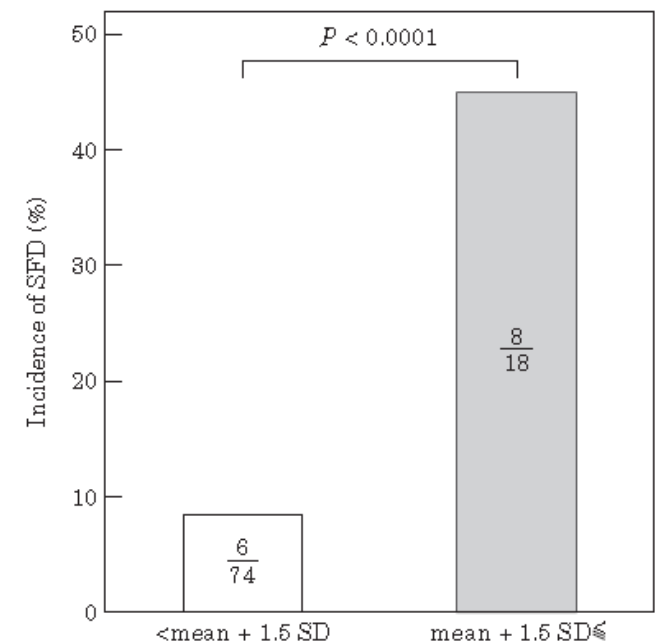
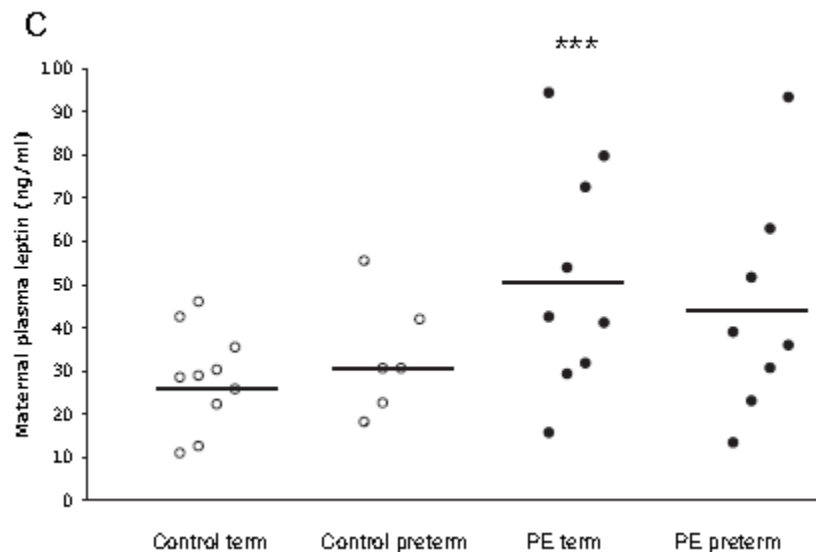
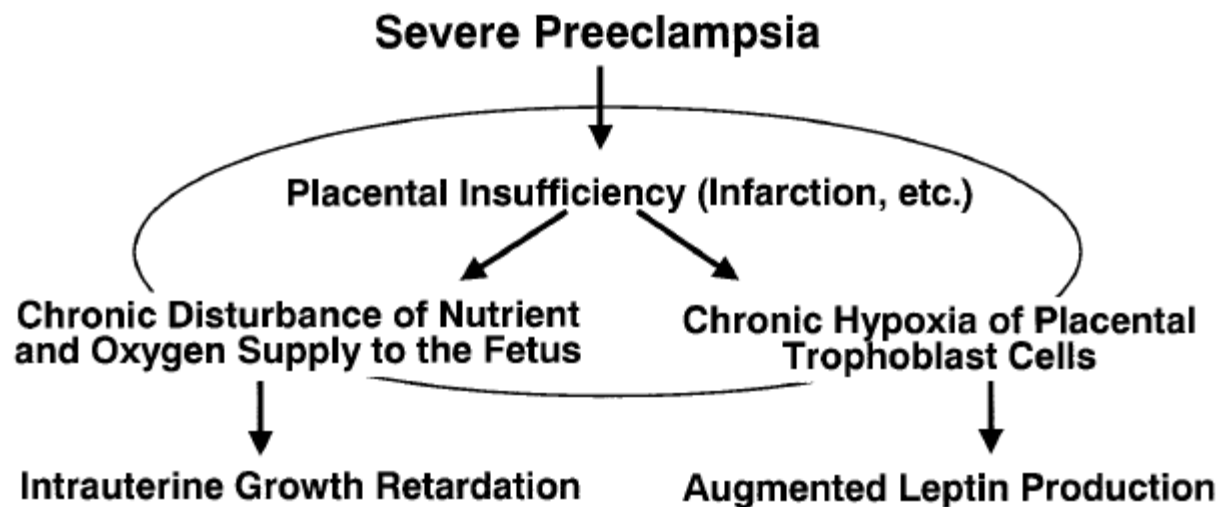


Table 4 Associations of maternal C-reactive protein levels in early pregnancy with the risks of maternal pregnancy complications

C-reactive protein level	No. of mothers	No. of cases	Model A [odds ratio (95% CI)]	Model B [odds ratio (95% CI)]	Model C [odds ratio (95% CI)]
Preeclampsia					
<5.0 mg/l	3001	53	Reference	Reference	Reference
5.0–9.9 mg/l	1485	27	1.03 (0.65–1.64)	1.09 (0.68–1.75)	0.81 (0.46–1.42)
10.0–14.9 mg/l	526	14	1.52 (0.84–2.76)	1.71 (0.93–3.13)	1.41 (0.71–2.80)
15.0–19.9 mg/l	188	7	2.15 (0.96–4.80)	2.41 (1.07–5.45) [†]	1.49 (0.54–4.16)
≥20.0 mg/l	229	5	1.24 (0.49–3.14)	1.38 (0.54–3.52)	0.61 (0.17–2.16)
Trend test			1.66 (1.02–2.71)	1.87 (1.13–3.09)	1.29 (0.75–2.22)
			<i>P</i> for trend 0.041	<i>P</i> for trend 0.015	<i>P</i> for trend 0.358

Values were based on multivariate logistic regression models and reflect the odds ratio (95% CI) for pregnancy complications for each C-reactive protein level group compared to the reference group (<5.0 mg/l). Model A was unadjusted. Model B was adjusted for gestational age at blood puncture, maternal age, education, ethnicity, parity, smoking and alcohol consumption. Model C was adjusted for gestational age at blood puncture, maternal age, education, ethnicity, parity, smoking, alcohol consumption and maternal BMI. Tests for trend were based on multiple linear regression models with the logarithmically transformed C-reactive protein as a continuous variable. CI, confidence interval. [†] *P* value < 0.05. [‡] *P* value < 0.01.

C-reactive protein levels, blood pressure and the risks of gestational hypertensive complications: The Generation R Study

Layla L. de Jonge^{a,b,c}, Eric A.P. Steegers^d, Gesina D.S. Ernst^{a,b,c}, Jan Lindemans^e, Henk Russcher^e, Albert Hofman^b and Vincent W.V. Jaddoe^{a,b,c}

Objectives Aim of this study was to investigate the associations of C-reactive protein levels, as marker of low-grade inflammation, with blood pressure development during pregnancy and the risks of gestational hypertensive complications. We also explored the role of maternal BMI in these associations.

Methods High-sensitivity C-reactive protein levels were measured in early pregnancy (median 13.2 weeks, 95% range 9.6–17.6) in 5816 mothers participating in a population-based prospective cohort study in the

After adjustment for maternal BMI, all associations attenuated.

Conclusion Our results suggest that first-trimester C-reactive protein levels are associated with SBP and DBP levels throughout pregnancy and with gestational hypertensive complications, but these associations are largely explained by maternal BMI. *J Hypertens* 29:2413–2421 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Journal of Hypertension 2011; 29:2413–2421

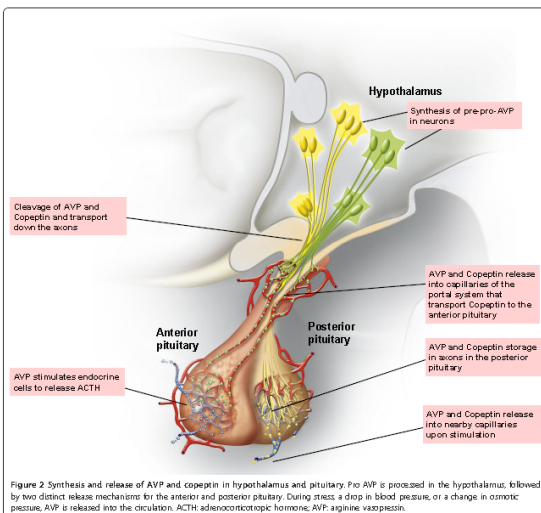


Table 2 Plasma copeptin levels and abnormal Doppler velocimetry in normotensive pregnant, mild pre-eclampsia and severe pre-eclampsia groups

	Normotensive pregnant (n = 32)	Mild pre-eclampsia (n = 32)	Severe pre-eclampsia (n = 32)
Maternal copeptin (ng/mL)	0.31 ± 0.09*	0.62 ± 0.16†	0.85 ± 0.18‡
Abnormal Doppler velocimetry n (%)	–	7 (21.87%)*	20 (62.5%)†

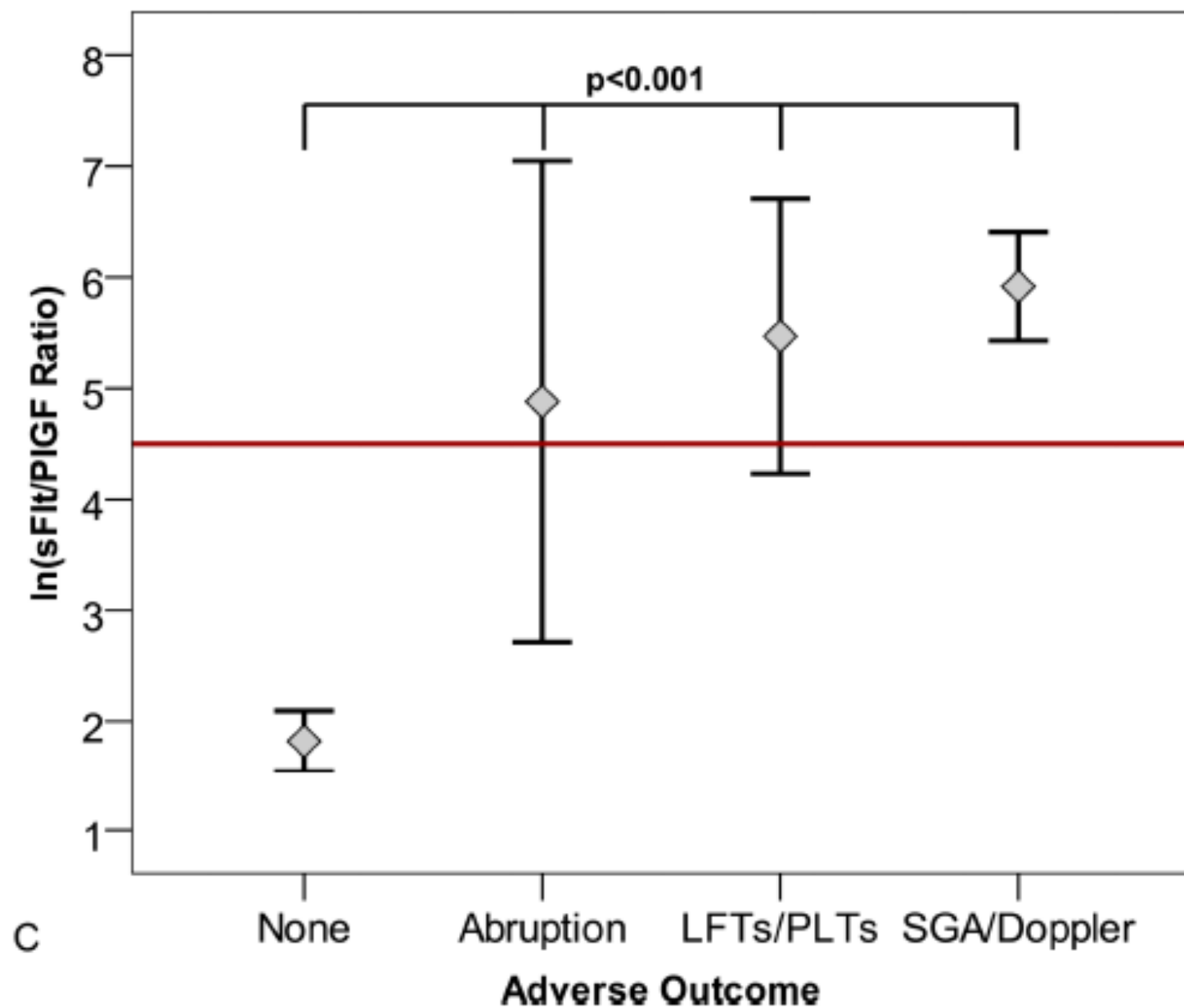
Values are mean ± SD. *, †, ‡ Groups with different symbols are significantly different from each other.

Table 3 Normal and abnormal Doppler velocimetry in relation to copeptin levels in pre-eclamptic patients

	Normal Doppler velocimetry (n = 37)	Abnormal Doppler velocimetry (n = 27)
Maternal copeptin (ng/mL)	0.73 ± 0.12	0.95 ± 0.14*

Values are mean ± SD. *Groups with different symbols are significantly different from each other.

Circulating levels of copeptin, a novel biomarker in pre-eclampsia



Rappel pour ne pas mourir idiot...

Soit l'étude suivante :

	Femmes		
	PE +	PE-	total
Test +	25	25	50
Test -	5	45	50
total	30	70	100

Se : VP/PE+

Sp : VN/PE-

VPP : VP/Test+

VPN : VN/Test-

OR : $(VP \cdot VN) / (FP \cdot FN)$

RV+ : Se/1-Sp : chances de test + si PE+

RV- : 1-Se/Sp : chances de test+ si PE-

Rappel pour ne pas mourir idiot...

Soit l'étude suivante :

$$Se : 25/30 = 0,83$$

$$Sp : 45/70 = 0,64$$

$$VPP : 25/50 = 0,50$$

$$VPN : 45/50 = 0,90$$

$$OR : (25 \times 45) / (5 \times 25) = 9 \text{ (3,06-26,44)}$$

$$RV+ : Se / 1 - Sp : 2,3$$

$$RV- : 1 - Se / Sp : 0,47$$

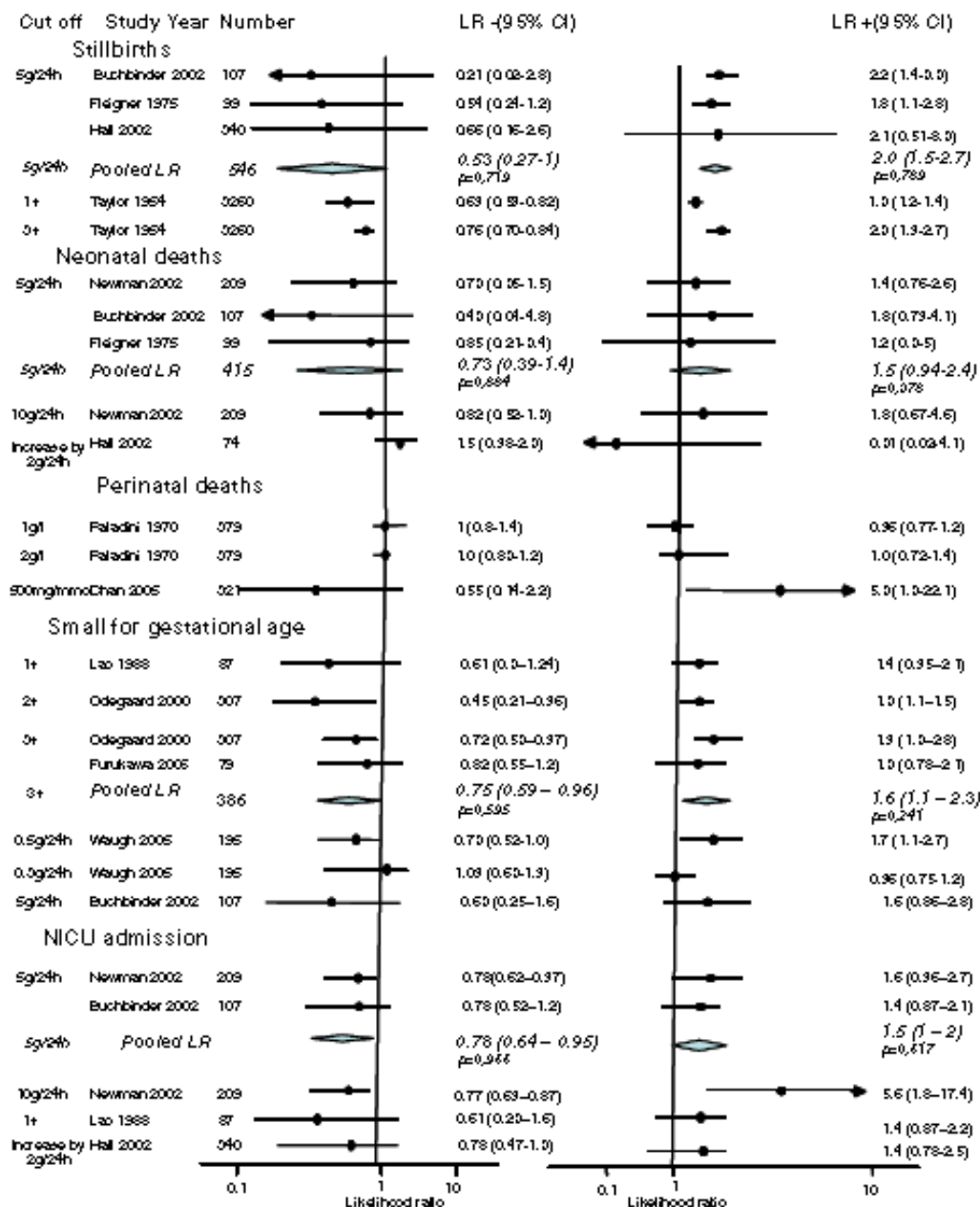
	Femmes		
	PE +	PE-	total
Test +	25	25	50
Test -	5	45	50
total	30	70	100

	Pré éclampsie	Grossesse Norm	
	N = 15	N = 11	
Plaquettes (G/L)	216 $\pm$ 45	264 $\pm$ 113	NS
Vol. plaq (fl)	9,8 $\pm$ 0,7	8,8 $\pm$ 1,2	p<0,01
IL 6	11 $\pm$ 24	2 $\pm$ 2	NS

European Journal of Clinical Investigation (2000) **30**, 1113–1118

The use of platelet density and volume measurements to estimate the severity of pre-eclampsia

P. Järemo, T. L. Lindahl, C. Lennmarken and H. Forsgren
Vrimevårdskliniken, Norrköping, Sweden



Protéinurie et complications néonatales

BMC Medicine

Research article

Estimation of proteinuria as a predictor of complications of pre-eclampsia: a systematic review

Shakila Thangaratnam^{*1}, Arri Coomarasamy¹, Fidelma O'Mahony², Steve Sharp³, Javier Zamora⁴, Khalid S Khan¹ and Khaled MK Ismail²



Open Access

Table 3. Accuracies of soluble endoglin (sEnd) and other urine analytes for the diagnosis of pre-eclampsia and the prediction of early delivery

Analyte	ROC area (95% CI)	P value	Cut-off*	Sensitivity (95% CI)	Specificity (95% CI)	+LR	LR	Accuracy
Diagnosis of severe pre-eclampsia (study population n = 234)								
sEnd (pg/mgc)	0.75 (0.76 0.88)	<0.001	>87.5	67 (59 75)	74 (64 83)	2.6	0.4	70.1
Protein to creatinine ratio (mg/mgc)	0.58 (0.54 0.60)	0.034	>10.6	44 (36 53)	77 (67 85)	1.9	0.7	56.8
uFlt/PIGF ratio	0.88 (0.88 0.96)	<0.001	>2.1	74 (66 81)	89 (81 95)	6.7	0.3	80.1
uFlt/PIGF ratio >2.1 and sEnd >87.5	NA	<0.001	NA	54 (46 62)	90 (84 96)	5.4	0.5	68.0
Diagnosis of severe pre-eclampsia at <37 weeks (study population n = 160)								
sEnd (pg/mgc)	0.83 (0.77 0.89)	<0.001	>87.5	70 (60 79)	86 (75 94)	5.2	0.3	76.3
Protein to creatinine ratio (mg/mgc)	0.62 (0.55 0.70)	0.039	>10.6	47 (38 58)	85 (73 93)	3.1	0.6	61.2
uFlt/PIGF ratio	0.94 (0.89 0.97)	<0.001	>1.5	97 (92 99)	80 (67 89)	4.8	0.1	90.6
uFlt/PIGF ratio >2.1 and sEnd >87.5	NA	<0.001	NA	69 (60 78)	95 (89 100)	13.6	0.3	78.7
Prediction of an indicated delivery for pre-eclampsia at <37 weeks (study population n = 160)								
sEnd (pg/mgc)	0.83 (0.77 0.89)	<0.001	>87.5	74 (64 82)	86 (75 93)	5.3	0.3	78.7
Protein to creatinine ratio (mg/mgc)	0.62 (0.55 0.70)	0.003	>10.6	48 (38 59)	83 (72 91)	2.9	0.6	62.5
uFlt/PIGF ratio	0.93 (0.88 0.97)	<0.001	>2.1	84 (75 91)	92 (83 97)	10.9	0.2	87.5
uFlt/PIGF ratio >2.1 and sEnd >87.5	NA	<0.001	NA	62 (52 72)	97 (93 100)	20.2	0.4	76.2

*Cut-off with the highest accuracy. +LR, positive likelihood ratio; LR, negative likelihood ratio; mgc, milligrams of creatinine; uFlt/PIGF ratio, urinary soluble fms-like tyrosine kinase 1 to placental growth factor ratio.