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Is there a correlation between maternal venous hemodynamic dysfunction and proteinuria of preeclampsia?

Tinne Mesens[a,*], Kathleen Tomsin[c], Anneleen S. Staelens[c], Jolien Oben[a], Geert Molenberghs[d], Wilfried Gyselaers[a,b]

[a] Dept. Obstetrics & Gynaecology, Ziekenhuis Oost Limburg, Genk, Belgium
[b] Dept. of Physiology, Hasselt University, Hasselt, Belgium
[c] Dept. Medicine and Life Sciences, Hasselt University, Hasselt, Belgium
[d] Centre for Medical Statistics, Hasselt University, Hasselt, Belgium

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ABSTRACT

Objectives: To evaluate in early and late preeclampsia a correlation of maternal venous Doppler flow characteristics with biochemical parameters in maternal serum and urine, or with gestational outcome.
Study design: In this observational cross-sectional study, renal interlobar vein impedance index (RIVI) was measured according to a standardised protocol for combined electrocardiogram-Doppler ultrasonography in 86 women with uncomplicated pregnancy, 78 women with late onset preeclampsia (≥34 w) and 67 with early onset preeclampsia (<34 w). For each group, maternal age, pre-gestational BMI and parity were recorded together with birth weight and –percentile. For both early onset and late onset preeclampsia, maternal serum was analysed for thrombocyte count and concentrations of creatinine, ASAT, ALAT and uric acid and 24 h urine collections were analysed for creatinine clearance and proteinuria (mg/24 h). A non-parametric Mann–Whitney *U*-tests was performed for continuous data and a Fisher's exact tests for categorical data. Significant linear dependence between variables was identified using Pearson's correlation coefficient at nominal level $a = 0.05$.
Results: Proteinuria was higher in early onset than in late onset preeclampsia (1756 mg [838–6116 mg] versus 877 mg [416–1696 mg], $p < 0.001$), and this was also true for RIVI in both left (0.45 [0.40–0.55] versus 0.41 [0.35–0.45], $p = 0.001$) and right kidney (0.45 [0.39–0.55] versus 0.38 [0.30–0.43], $p < 0.001$). In our data set, there was a significant correlation between proteinuria and RIVI of left (correlation coefficient = 0.172, $p = 0.036$) and right kidney (correlation coefficient = 0.218, $p = 0.009$) in late onset but not early onset preeclampsia.
Conclusion: Maternal RIVI may correlate with proteinuria of late onset preeclampsia.

Introduction

During pregnancy, the maternal circulation adapts to an initial fall in total peripheral vascular resistance by initiating a high flow/low resistance circulation in combination with plasma volume expansion [1]. Duplex ultrasound scanning of the maternal vessels provides a non-invasive, useful tool to obtain more information on normal and pathological gestational hemodynamic mechanisms.

In the maternal venous compartment, different patterns of Doppler waves have been observed in the kidneys at the level of the renal interlobar veins and in the hepatic veins during normal pregnancy; i.e. pulsatile, intermediate and uniform waveforms [2–5]. The pulsatile type is observed more frequently in early gestation and in postpartum, whereas the uniform or flat types are mainly present in uncomplicated third trimester pregnancies. Standardization of Doppler methodology, the association of the maternal electrocardiogram (ECG) to the Doppler image and the use of repeated measures have been reported to improve venous Doppler wave interpretation [6,7]. The renal interlobar vein impedance index (RIVI) is considered to be the equivalent of the arterial resistance index, and is defined as [MaxVelocity – MinVelocity)/MaxVelocity]. The decrease in venous impedance in the kidneys and flattening of the hepatic venous wave form coincide with the known reduction in peripheral vascular resistance, the increased intravascular blood volume and the rise of abdominal pressure during pregnancy [2,8,9].

* Corresponding author. Tel.: +032 89 32 75 49; fax: +032 89 32 79 20.
E-mail address: tinne.mesens@zol.be (T. Mesens).

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RIVI is reported to be higher in preeclampsia than in uncomplicated pregnancies, and this effect is more pronounced at <34 weeks than near term [10]. This observation corresponds with the definition of two types of preeclampsia: early-onset (<34 weeks) and late-onset (>34 weeks) preeclampsia, both presenting with different cardiovascular characteristics [11–13].

In this observational study, we tested the hypothesis that different renal interlobar vein Doppler characteristics in early- and late-onset preeclampsia correlate with different maternal serum and urine parameters, and with gestational outcome.

Materials and methods

Approval of the ethical committee was obtained before study onset (MEC ZOL reference: 06/043, 08/049, 09/049 and 10/065).

The hospital register of the Maternal Fetal Medicine Unit of Ziekenhuis Oost-Limburg, Genk Belgium, was searched to identify those women, admitted for preeclampsia between 01/01/2006 and 31/12/2011. Only singleton pregnancies of women without known pre-existing diseases, such as juvenile diabetes, lupus erythematosus or rheumatic diseases, clotting disorders or other liver, kidney and cardiovascular disorders were included. In addition to this, a group of women with normal early or late third trimester pregnancies were selected randomly at the outpatient clinic of the same hospital. These patients were enrolled as part of an ongoing prospective study of the physiological changes of pregnancy [10] and were used as a control group for this study. Preeclampsia was defined as new onset gestational hypertension (≥140/90 mmHg) with de novo proteinuria (≥300 mg/24 h) without thrombocytopenia or liver dysfunction, according to the criteria of the National High Blood Pressure Education Program Working Group [14,15]. All normal pregnancies and those complicated with preeclampsia were also categorized in 2 major classes, according to gestational age at diagnosis: <34 weeks and ≥34 weeks. As such, there were 4 categories eligible for analysis: uncomplicated pregnancies <34 weeks, early onset preeclampsia <34 weeks, late uncomplicated pregnancies ≥34 weeks and late onset preeclampsia ≥34 weeks.

For each woman, data on demographics, perinatal outcome and maternal venous Doppler parameters of both kidneys were recorded at the time of admission. For preeclamptic patients, serum and urine biochemistry was also recorded. Maternal demographic data include age, body mass index (BMI) at beginning of pregnancy, and parity. Data on perinatal outcome comprise gestational age at delivery (weeks), birth weight (BW in g) and customized birth weight percentile (BW% in %). Serum parameters include thrombocytes (1000/μL), creatinine (mg/dL), aspartate aminotransferase (ASAT in U/L), alanine aminotransferase (ALAT in U/L), and uric acid (mg/dL). Parameters evaluated in 24 h urine collections at the time of diagnosis of preeclampsia were creatinine clearance (mL/min), and proteinuria over 24 h (mg). All women had Doppler sonographic assessment of maternal hemodynamics at the levels of renal interlobar veins. All examinations were done by 3 sonographers (TM, KT, WG) according to the protocol reported elsewhere [3,10], with known intra- and interobserver correlation [6]. Doppler parameters measured at the level of renal interlobar veins were maximum velocity (MxV) and minimum velocity (MinV). From this, RIVI was calculated as [(MxV − MinV)/MxV] [16]. Hepatic vein Doppler measurements or venous pulse transit times were not considered in this study.

A non-parametric Mann–Whitney *U*-tests was used for continuous data and Fisher's exact tests for categorical data. Data are presented as medians (25th percentile; 75th percentile) or percentages. Significant linear dependence between variables was identified using Pearson's correlation coefficient (PCC) at nominal level $\alpha = 0.05$ (two-tailed). All statistical analyses were done using the SPSS package, software version 20.0.

Results

A total of 231 women were included: 145 women had preeclampsia of which 67 were diagnosed before 34 weeks and 78 after 34 weeks. The other 86 women had uncomplicated pregnancies; 46 were evaluated before and 40 others at gestation later than 34 weeks. All women with preeclampsia had serum tests and 24 h urine collections.

Table 1
Demographic characteristics, lab results and Doppler-derived impedance indices of renal interlobar (RIVI) maternal veins. Data are shown as median (25th percentile; 75th percentile) or percentage. Early: <34 w; Late: ≥34 w; UP: uncomplicated pregnancy; PE: preeclampsia; BMI: body mass index; Gest.age: gestational age; CreatS: Serum creatinin; ASAT: aspartate aminotransferase; ALAT: alanine aminotransferase; CreatCl: creatinin clearance; ProtU/24 h: 24 h proteinuria; LK: left kidney, RK: right kidney.

	Early UP $n=46$	vs p-Value	Early PE $n=67$	vs p-Value	Late PE $n=78$	vs p-Value	Late UP $n=40$
			Demographics				
Maternal							
Age (years)	30 (27;32)	0.211	28 (26;31)	0.682	29 (26;32)	0.036	31 (28;33)
Pre-gestational BMI	23 (22;26) ($n=41$)	0.047	26 (23;29) ($n=43$)	0.873	25 (23;31) ($n=70$)	0.019	23 (22;25) ($n=37$)
Nulliparity	21 (46%)	0.005	48 (72%)	0.296	63 (77%)	0.001	18 (45%)
Neonatal							
Gest.age (weeks)	39 (38;40)	<0.001	32 (29;33)	<0.001	37 (36;39)	<0.001	39 (38;40)
Birth weight (g)	3225 (2918;3535)	<0.001	1428 (993;1726)	<0.001	2845 (2513;3343)	<0.001	3213 (3003;3459)
Birth weight (%)	50 (25;75)	<0.001	22 (10;38)	0.006	38 (18;60)	0.221	44 (25;63)
			Lab results				
Blood							
Trombocytes (1000/μL)		209 (167;279)	0.743	214 (172;264)			
CreatS (mg/dL)		0.68(0.60;0.81)	0.294	0.67(0.58;0.74)			
ASAT (U/L)		18 (15;27)	0.809	19 (16;24)			
ALAT (U/L)		13 (10;22)	0.094	11 (8;18)			
Uric Acid (mg/dL)		6.4(5.4;7.1)	0.054	6.0(5.0;6.9)			
Urine							
CreatCl (mL/min)		117(93;147)	0.433	121(96;151)			
ProtU/24 h (mg)		1756 (838;6116)	<0.001	877 (416;1696)			
Renal Doppler parameters							
LK RIVI	0.40 (0.33;0.44)	<0.001	0.45 (0.40;0.55)	0.001	0.41 (0.35;0.45)	0.260	0.39 (0.33;0.45)
RK RIVI	0.31 (0.29;0.36)	<0.001	0.45 (0.39;0.55)	<0.001	0.38 (0.30;0.43)	<0.001	0.30 (0.27;0.35)
Interrenal difference	0.07 (0.01;0.11)	0.001	0.01 (−0.05;0.07)	0.154	0.03 (−0.03;0.10)	0.007	0.08 (0.03;0.13)

In this observational cross-sectional study, a significant correlation between proteinuria and maternal renal vein impedance index is seen in late onset preeclampsia.