Doppler Echo-flowmetry of the Uterine District and Peeclampsia

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ABSTRACT---- ***The Authors prospectively determined the uterine artery Doppler flow velocimetry between the 10th and 13th week of pregnancy in 32 women with history of HDP (Hypertensive Disorder of Pregnancy) in the attempt to identify those at higher risk to develop preeclampsia during the ongoing pregnancy and the need for prophylactic pharmacological treatment. Patients with abnormal flowmetric values (RI > 0.58) were immediately started on aspirin 100 mg/daily followed at the 24th week by daily subcutaneous injection of low molecular weight heparin. The authors found that the average pregnancy course in terms of maternal morbidity (expressed by abnormal blood pressure and 24 hour proteinuria) in 20 prophylactic treated patients with abnormal 1st trimester uterine artery flowmetry was better than in their previous pregnancies, however in relation to the above parameters no significant difference was found between the patients treated and those (n =12) with normal I trimester uterine artery Doppler flowmetry who were also followed till delivery and 6 weeks post partum but not prophylactic treated. The study suggests that uterine artery flow velocimetry determination in the late first trimester of pregnancy is useful in reducing the risk of preeclampsia especially in patients with previous history of HDP allowing the prompt institution of prophylactic treatment in selected patients.***

1. INTRODUCTION

Preeclampsia (PE) is a multisystemic disorders that provoke a great number of maternal deaths worldwide. [1]

It is recognized as the 3rd cause of direct maternal mortality. PE risk factors are: elevated body mass index, maternal age extremes and Afro-American ethnicity; besides, some diseases such as diabetes and chronic hypertension also significantly increase the risk.[2-3]

Today it's well known that Preeclampsia is a disease affecting the vascular endotelium. A regularly evolving pregnancy is characterized by a preserved endothelial function and a progressive reduction in the resistance of uterine vessels, due to the placentation process.

An inadequate trophoblastic invasion and the consequent poor placentation are the key mechanisms of PE physiopathology. [4-7]

The systemic endothelial dysfunction, leading to thrombotic phenomenon in the microcirculation, reduces the perfusion of tissues and organs, including the placenta itself, creating an even more hypoxemic environment. Chronic placental hypoxia causes both oxidative stress with consequent placental apoptosis and necrosis and to an increased expression of proinflammatory, antiangiogenic, and angiogenic factors, amplifying the systemic endothelial impairment.

A good endotelial function and an optimal vascular dilatation are extremely important for an healthy gestation. Without these conditions both maternal and fetal prognosis is compromised. [8]

According to the recent literature [2], perinatal and maternal morbidity and mortality due to pre-eclampsia may be reduced through an early diagnosis and treatment.

Prediction of early Pre-eclampsia (clinical symptoms before 34 weeks of pregnancy) is possible by searching for some circulating factors (PAI-I and fibroadectin) or by determining the uterine arteries pulsatility index (UtA-PI) during the second trimester.

The use of UtA-PI alone in the second trimester of pregnancy allows to detect almost 95% of all cases of early PE[10], the uterine arteries bilateral notch is able to outline not only patients that subsequently develop PE, but also those whose pregnancies will be complicated by intrauterine growth restriction (IUGR).[11-12]

The Authors investigated the role of earlier determination of UtA-PI, during the late 1st trimester of pregnancy (from 11^{+0} to 13^{+6} gestational week) in the management of pregnancy in patients with history of preeclampsia. [9]

2. MATERIALS & METHODS

The aim of this study is to conduct a careful quantitative and morphological analysis of the pulsatile waves of uterine arteries in patients with HDP (Hypertensive Disorders in Pregnancy) risk, to eventually submit them to appropriate therapy.
The diastolic wave reduction, the resulting relative systolic-diastolic ratio (resistance index, RI) increase, the image of a "notch" between the systolic and diastolic components would be the expression of increased uterine resistance, which usually represents the first stage in the increase of peripheral resistance (fig.1, fig.2).The examination is simple and noninvasive, repeatable, and therefore it takes place in a very short time.

The Authors enrolled for the study 32 patients at risk of hypertensive disorders in pregnancy (HDP) who, for this reason, were examined at the outpatient clinic of "Ospedale Santo Bambino" in Catania. Characteristics of enrolled patients are shown in tab.1 and tab.2. The patients' mean age was 30 ± 0,4 years, BMI was 25 ± 0,2kg/m2 and all patients had a history of gestational hypertension in her previous pregnancy. All women underwent Doppler flowmetry of the uterine arteries between the 10-13 week of pregnancy, using a 3.5 MHz multi frequency probe.

In 20 patients (Group A) an increased RI (> 0.58) and a characteristic bilateral notch were found (tab. 3). 12 patients (Group B) showed no flowmetric alterations (tab. 4).

Group A patients were treated with aspirin (100 mg daily) until the 24th week and, subsequently switched to subcutaneous low molecular weight heparin (4.000 I.U. daily), and started to close clinical and ultrasound follow-up (every 15 days) for the assessment of fetal and maternal wellbeing till delivery. During the puerperal hospital stay and 6 weeks postpartum they were also re-evaluated for signs and symptoms of hypertensive disorders.

Group B patients, although not subjected to any prophylactic treatment ,were also followed in the same manner as group A patients.

Figure 1. Normal uterine artery Doppler flowmetry

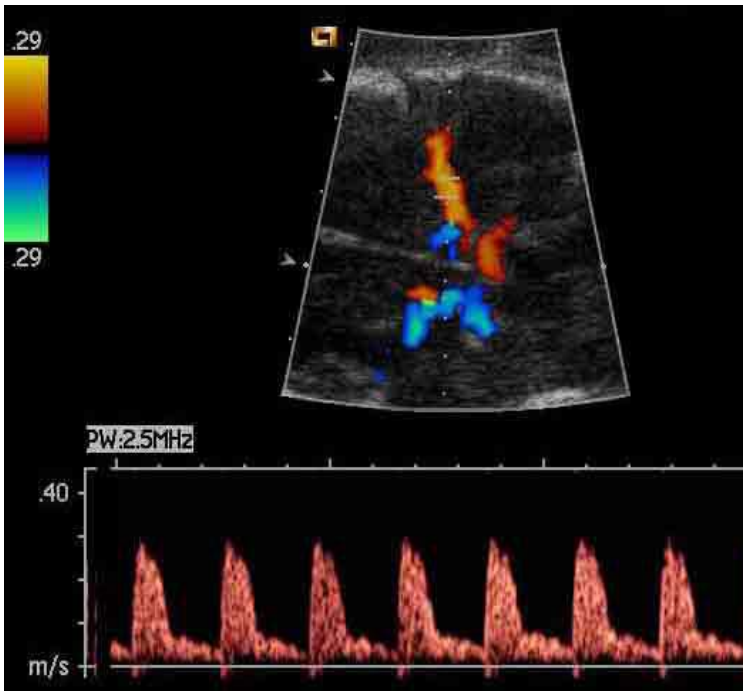
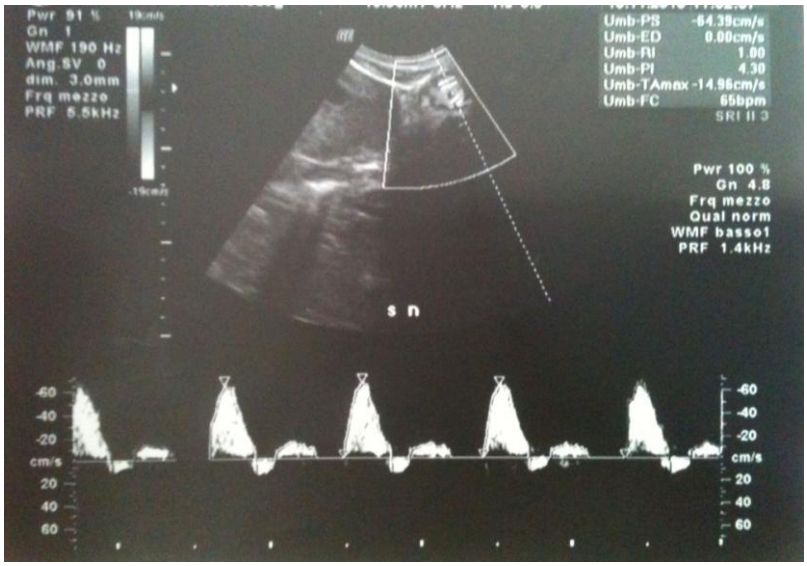


Figure 2. Abnormal uterine artery Doppler flowmetry



II and III trimester mean blood pressure and mean 24hour proteinuria determined for each group A patient during the ongoing pregnancy was compared with that reported by the same patient during the previous pregnancy, the one complicated by the hypertensive disorder. The Authors also evaluated maternal and perinatal outcome regarding only the present pregnancy in group B patients and related to both the previous and last pregnancy in group A patients.
Statistical analysis was carried out using t di Student test.

3. RESULTS

All patients considered in Group A had an excellent outcome both maternal (blood pressure <130/90 mmHg and mean 24h proteinuria <300 mg throughout pregnancy) and neonatal (no cases of IUGR, intrauterine growth restriction , mean neonatal weight: 3.100 ± 200 g with good Apgar scores).

Group A patients had a mean B.P. and a mean 24hour proteinuria essentially normal and significantly lower, especially in the III trimester, than those reported during their previous pregnancy ($p<0.05$) (tab. 5-6).

Regarding Group B, 2 patients developed a mild grade of preeclampsia during

the 34th week of pregnancy with a complete resolution 6 weeks post-partum (tab. 7).

The authors found that the average pregnancy course (maternal morbidity) in the 20

prophylactic treated patients with abnormal 1st trimester uterine artery flowmetry was

significantly better than in their previous pregnancies ($p<0.05$) (tab. 5 and tab. 6), no significant difference in maternal morbidity was found between the patients treated and those (tab.4) with normal I trimester uterine artery Doppler flowmetry who were also followed till delivery but not prophylactic treated.

Similar overall perinatal outcome was observed between the two group of patients and in group A patient between the present pregnancy and the previous one.

4. DISCUSSION AND CONCLUSIONS

The presence of a bilateral notch should be considered to be highly predictive of subsequent preeclampsia (RR = 21.99, sensitivity 92.9%, specificity 85.1%) at early gestational age (10-13 weeks), as at 24th week (sensitivity 81.2%, positive predictive value 27%).[13]

Using a cut-off of RI > 0.58 a high predictive value is identified with 63% of sensitivity and a positive predictive value of 70%.

The early measurement of the resistance of arcuate arteries could, therefore, reveals an impaired trophoblastic invasion of the uterine arteries, holding a high predictive power, and offering the possibility to evaluate the uterine and fetal district longitudinally, by monitoring the effects of the disease over time.

In Literature there are various data that are discordant from each other.

Some Authors says that UADV and maternal serum PlGF (placental growth factor) estimation at 20-22 weeks of gestation are strong predictors of the occurrence of pre-eclampsia when used individually but together their association with pre-eclampsia is not significant. [14]

Other Authors, on the other side, assert that in models using maternal history and 11-14 weeks-UAD, the negative predictive value is high, while abnormal UAD may identify an equally high proportion of women that will develop early-onset preeclampsia. Besides, they believe that algorithms combining biochemical markers could still improve this prediction rate at higher cost and complexity. [15]

Maternal plasma PAI-1 (human Plasminogen Activator Inhibitor) combined with fibronectin seems to have the highest predictive value for preeclampsia.[16]

The Authors found that patients with HDP risk and abnormal uterine artery Doppler flowmetry didn't develop hypertension or preeclampsia in the ongoing pregnancy, most probably because of the treatment with aspirin and LMWH.

Furthermore the study demonstrated that uterine artery flow velocimetry determination in the late first trimester of pregnancy may be useful in reducing the risk of preeclampsia especially in patients with previous history of HDP allowing the prompt institution of prophylactic treatment in selected patients.

Although the present study, based on a restricted number of patients, does show that prophylactic treatment has a significant impact only on maternal morbidity without changing the overall maternal and perinatal outcome, probably by recruiting larger number of patients, prophylactic treated and non, the observed reduction in maternal morbidity could also affect maternal and perinatal long term morbidity and mortality.

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Table 1. Patients characteristics (Group A)

	Age	Parity	BMI	Comorbidity	Previuos HDP	Family Hystory of Hypertension
1	32	1	28	hypothyroidism	X	Grandmother
2	26	2	20	--	X	--
3	30	1	24	--	X	--
4	28	1	23	--	X	--
5	38	3	28	--	X	Father and mother
6	24	1	19	--	X	--
7	30	1	26	Sinus tachycardia	X	Mother
8	29	1	28	--	X	--
9	35	2	28	--	X	--
10	40	3	30	Diabetes type I	X	Mother
11	33	2	23	--	X	--
12	26	1	24	--	X	Father and mother
13	28	1	22	--	X	--
14	32	1	29	--	X	Mother
15	32	2	22	Hypothyroidism	X	--
16	27	1	28	--	X	--
17	29	1	26	--	X	--
18	32	2	28	--	X	--
19	31	1	23	--	X	--
20	25	2	25	--	X	Sister

Table 2. Patients characteristics (Group B)

	Age	Parity	BMI	Comorbidity	Previous HDP	Family Hystory of Hypertension
1	30	1	25	--	X	--
2	32	2	28	--	X	Sister and mother
3	26	1	23	Hypothyroidism	X	--
4	28	1	22	--	X	--
5	24	1	30	--	X	--
6	36	2	24	--	X	Mother
7	30	1	25	Hypothyroidism	X	--
8	28	1	28	--	X	--
9	31	2	22	--	X	--
10	23	1	25	--	X	--
11	39	3	24	Diabetes type II	X	Mother
12	30	1	26	--	X	mother

Table 3. Uterine artery flowmetric values (Group A)

Patient	RI value
1	0,83
2	0,60
3	0,65
4	0,63
5	0,80
6	0,78
7	0,60
8	0,61
9	0,61
10	0,62
11	0,72
12	0,65
13	0,76
14	0,66
15	0,70
16	0,80
17	0,65
18	0,68
19	0,84
20	0,81

Table 4. Uterine artery flowmetric values (Group B)

Patient	RI value
1	0,58
2	0,50
3	0,55
4	0,53
5	0,50
6	0,48
7	0,50
8	0,51
9	0,51
10	0,52
11	0,52
12	0,55

Table 5. Previous pregnancy with HDP (Group A)

	II trimester		III trimester				
	Mean B.P.	Mean 24h Proteinuria (mg)	Mean B.P.	Mean Proteinuria (mg)	Term birth	Newborn weight (g)	Apgar
1	130/90	<300	160/90	550	36	2500	8
2	125/80	<300	145/90	350	37	2950	10
3	110/70	<300	145/95	400	37	3100	9
4	100/85	<300	140/80	<300	38	3000	9
5	130/80	<300	155/90	500	39	3300	10
6	120/85	<300	150/80	450	38	3025	10
7	125/90	<300	150/95	650	36	3120	10
8	110/70	<300	145/90	<300	38	3100	10
9	100/60	<300	150/90	500	38	2980	9
10	130/85	<300	160/95	650	36	2450	8
11	90/50	<300	145/90	450	38	3080	9
12	120/80	<300	150/90	500	37	3060	9
13	120/85	<300	150/85	450	39	3200	10
14	125/85	<300	145/90	450	39	3100	10
15	125/85	<300	145/90	400	39	3000	9
16	110/60	<300	140/100	800	36	2600	9
17	100/70	<300	150/90	500	38	3100	10
18	120/70	<300	145/95	550	37	3050	10
19	130/85	<300	160/90	700	36	2600	8
20	120/85	<300	150/90	750	36	2650	8

Table 6. Ongoing pregnancy with prophylactic treatment (Group A)

	II trimester		III trimester				
	Mean B.P.	Mean 24h Proteinuria (mg)	Mean B.P.	Mean Proteinuria (mg)	Term birth	Newborn weight (g)	Apgar
1	120/80	<300	120/80	<300	38	2500	8
2	125/80	<300	125/90	<300	39	2950	10
3	100/70	<300	125/80	<300	39	3100	9
4	100/70	<300	110/70	<300	39	3000	9
5	110/80	<300	120/80	<300	40	3300	10
6	120/75	<300	120/70	<300	39	3025	10
7	125/80	<300	125/70	<300	38	3120	10
8	100/65	<300	110/80	<300	39	3100	10
9	100/60	<300	120/80	<300	39	2980	9
10	110/75	<300	120/80	<300	38	2450	8
11	90/50	<300	100/70	<300	39	3080	9
12	120/80	<300	120/85	<300	39	3060	9
13	120/80	<300	120/80	<300	40	3200	10
14	125/70	<300	125/80	<300	40	3100	10
15	110/70	<300	120/60	<300	40	3000	9
16	110/60	<300	120/85	<300	39	2600	9
17	100/70	<300	110/70	<300	41	3100	10
18	120/70	<300	100/65	<300	39	3050	10
19	120/60	<300	120/80	<300	39	2600	8
20	120/75	<300	120/80	<300	38	2650	8

Table 7. Ongoing pregnancy without prophylactic treatment (Group B)

	II trimester		III trimester				
	Mean B.P.	Mean 24h Proteinuria (mg)	Mean B.P.	Mean Proteinuria (mg)	Term birth	Newborn weight (g)	Apgar
1	110/80	<300	120/80	<300	38	2900	9
2	95/60	<300	125/90	<300	39	3050	10
3	90/50	<300	125/80	<300	39	3200	10
4	120/80	<300	170/100	650	36	2005	8
5	100/70	<300	120/80	<300	40	3400	10
6	110/70	<300	120/70	<300	39	3125	10
7	105/60	<300	125/70	<300	38	3320	10
8	120/85	<300	160/100	500	37	2100	8
9	100/60	<300	120/80	<300	39	2980	9
10	110/70	<300	120/80	<300	38	3450	9
11	110/75	<300	100/70	<300	39	3180	9
12	120/80	<300	120/85	<300	39	3260	9