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Maternal Total Vascular Resistance: A New Parameter to Identify Hypertensive Pregnancy Complications

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Abstract

Introduction: Maternal cardiovascular system adapts to pregnancy thanks to complex physiological mechanisms that involve cardiac output and total vascular resistance. Abnormalities of this adaptive mechanisms are connected with hypertensive disorders.

Materials and methods: We enrolled 140 healthy normotensive women during the first trimester of pregnancy obtaining all measurements with the USCOM system, a non invasive method. All patients were subsequently evaluated at 16 and 22-23 weeks of gestation and were followed until the end of pregnancy to check for fetal-neonatal and maternal outcomes.

Results: Patients were retrospectively divided in two groups: Group A (n = 37): patients with TVR values persistently elevated at 22 weeks of gestation (>1200 dyne/sec/cm-^{5}) and Group B (n = 103): patients with a reduction of TVR values at 22 weeks of gestation (<1200 dyne/sec/cm-^{5}).

Among the group A, 7 patients developed gestational hypertension, 3 patients developed preeclampsia and 5 pregnancies were complicated by intrauterine growth restriction. In the Group B there is an increase in Stroke Volume and Cardiac Output; the last one result could be a compensation response ensuring a proper peripheral vascular filling.

Discussion: The introduction of USCOM has provided non invasive means for the evaluation of maternal cardiovascular adaptation. Our data showed that into 37 patients group (26.5% of the total) with persistently elevated TVR values at 22-23 weeks, 15 women (10% of the total) experienced hypertensive complications. According to our data, a maternal hemodynamic condition characterized by persistently elevated TVR values in the second trimester of pregnancy probably represents a risk factor for a poor fetal-maternal outcome representing a high-risk group of pregnant women that need to be strictly monitored.

Conclusion: TVR might help to identify pregnant women at high risk of developing hypertensive complications.

Keywords: *Total Vascular Resistance; pregnancy induced hypertension; preeclampsia; USCOM; placental maladaptation*

Introduction

In recent years maternal cardiac function was studied in normal and complicated pregnancy obtaining important information on systolic and diastolic function and on morphological parameters of the left ventricle [1].

During pregnancy maternal hemodynamics undergoes important physiological adaptations to ensure an adequate uteroplacental perfusion and to promote normal fetal development. In physiological pregnancies because of the remodelling of the spiral artery there is a reduction in uteroplacental resistance index associated with a decrease of the Total Vascular Resistance (TVR) which represents the steady component of the afterload and includes the uteroplacental circulation with a contribution of 20% to 26% to the total reduction of systemic vascular resistance in the second trimester [2].

Associated with the decline in Total Vascular Resistance (TVR) there is an increase in Cardiac Output (CO) and Stroke Volume (SV). These changes take place during early phases of pregnancy: since the 5th week and most of TVR fall (85 %) is seen at 16 weeks of gestation [3,4].

The lack of these hemodynamic changes seems to be correlated with an increased risk of pregnancy complications, such as pregnancy induced hypertension (PIH), preeclampsia (PE) and fetal growth restriction (FGR) [5].

Aim of this study is to analyse Total Vascular Resistance trend in the first and second trimester of pregnancy as a sign of maternal cardiovascular adaptation to pregnancy. The finding of high TVR values during the first and second trimester of pregnancy may indicate an abnormal vascular adaptation that might expose to a higher risk of complications.

Materials and Methods

An observational study was conducted at the San Giovanni Calibita Fatebenefratelli Hospital, Department of Obstetrics and Gynaecology in Rome over a continuous period from November 2011 to December 2012. Approval of the local ethics committee was obtained based on a submitted protocol, and informed consent was obtained from all patients prior to enrolment.

We enrolled 140 healthy, normotensive pregnant women during the first trimester of pregnancy (from 5+0 to 11+6 weeks of gestation) at their first check. All patients were subsequently evaluated at 16 and 22-23 weeks of gestation. We monitored maternal hemodynamics throughout the USCOM 1A (Ultrasonic Cardiac Output Monitor, Uscom Limited, Sydney, Australia), a non-invasive monitoring technology.

We retrospectively divided the study population in two groups:

Group A (n = 37): patients with TVR values persistently elevated at 22 weeks of gestation (> 1200 dyne/sec/cm^{-5})

Group B (n = 103): patients with a reduction of TVR values at 22 weeks of gestation (< 1200 dyne/sec/cm^{-5}).

All patients were followed until the end of pregnancy to check for fetal-neonatal and maternal outcomes. Hypertensive disorders in pregnancy, as already mentioned by Larciprete and Montagnoli [6], was diagnosed according to the definition of ISSHP [7]: (1) preeclampsia: de novo hypertension (systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg) after 20 wk of gestation associated with proteinuria. Proteinuria is defined as appearance of urinary protein greater than 300 mg/dl or a spot urine protein/dreatinine ratio ≥ 30 mg/mmol; (2) gestational hypertension: de novo hypertension alone after 20 wk of gestation; (3) chronic hypertension: hypertension diagnosed before 20 wk of gestation or preconception hypertension; (4) preeclampsia superimposed on chronic hypertension: in a woman with chronic hypertension, development of proteinuria and/or symptoms associated with preeclampsia after 20 wk of gestation.

Intrauterine Growth Restriction refers to a fetus with an estimated fetal weight < 10th percentile on ultrasound that, because of a pathologic process, has not attained its biologically determined growth potential [8].

Haemodynamic measurement

All haemodynamic measurements were acquired with the USCOM 1A. The USCOM has been validated against invasive gold standards and flow probes and has proof of effectiveness in pre-eclampsia [9-11]. USCOM uses continuous-wave Doppler to determine CO by a non-imaging transducer placed at the suprasternal notch to measure transaortic or transpulmonary blood flow. To calculate CO the transducer is placed in the suprasternal notch or in parasternal inter space, and the Doppler beam directed across the aortic or pulmonary valve to acquire a spectral Doppler flow profile displayed as a time-velocity plot. Once the optimal flow profile is obtained, the trace is frozen on the screen, and the flow profiles automatically traced allowing the stroke volume (SV) to be calculated as the product of the velocity-time integral and the cross-sectional area (CSA) of the chosen valve. The CSA of the aortic valve is determined from the proprietary height-indexed regression equations. The CO is then calculated from the product of the heart rate (HR) and SV. Input of blood pressure provides for calculation of TVR. We recorded, CO, SV, HR, Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP). All patients were examined following signed informed consent in accordance with the ethical approval.

Results

	Group A	Group B	*p*
Age (years)	32.56 ± 5.67	33.90 ± 5.97	ns
Height (m)	1.65 ± 0.13	1.65 ± 0.10	ns
Weight (kg)	60.23 ± 4.5	61.31±5.6	ns
BMI (kg/m^2)	22.05 ± 2.1	22.42 ± 2.4	ns

Table 1: *Characteristics of study population.*

Table 2 shows the average values of the heamodynamic parameters at 22-23 weeks of gestation Among 37 patients (26.5% of the total) with persistent high TVR values (> 1200 dyne/sec/cm^{-5}) at 22-23 weeks of gestation, 15 women (10% of the total) developed complications (7 patientsgestational hypertension, 3 patients preeclampsia and 5 pregnancies were complicated by intrauterine growth restriction). Among 103 patients of group B (73, 5 % of the total), 9 patients (6% of the total) developed complications (5 patients gestational hypertension, 3 patients preeclampsia and 1 patient intrauterine growth restriction).

	Group A (22 wks)	Group B (22 wks)	*p*
Cardiac Output (L/min)	5.45 ± 0.66	7.64 ± 1.44	< 0.01
Total Vascular Resistance (dyne/sec/cm^{-5})	1350.62 ± 211.5	915 ± 162.89	< 0.01
Heart Rate (bpm)	74.12 ± 11.3	81.86 ±8.2	< 0.01
Stroke Volume (mL)	74.62 ± 14.7	93.27± 10.3	< 0.01
Systolic Blood Pressure (mmHg)	124 ± 9.93	113.5 ± 10.54	< 0.01
Diastolic Blood Pressure (mmHg)	73.75 ± 10.08	70.71 ± 6.61	ns

Table 2: *Hemodynamic features of study population at 22-23 weeks of gestation*

Figure 1 illustrates the TVR trend of the two groups of patients, since early pregnancy to 22 weeks of gestation. Group B shows a physiological decreasing trend of TVR at 22-23 weeks, the period in which vascular placental bed is considered fully completed. On the contrary, the other group of patients shows higher TVR values during the first weeks of gestation, a slight decrease at 16 weeks and a subsequent increase at 22-23 weeks (1350.62 ± 211.5 vs 915 ± 162.89 p < 0,01).

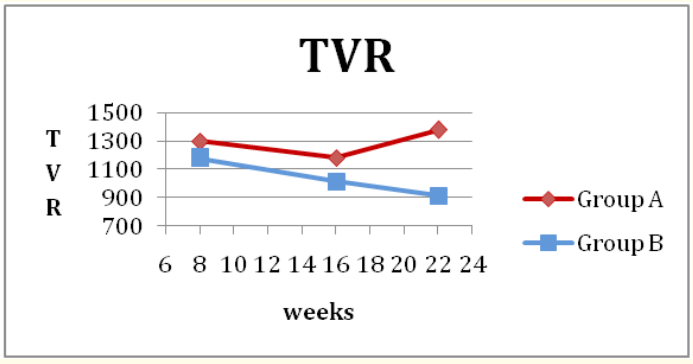

Figure 1: *TVR trend between the two groups.*

Figure 2 shows the Cardiac Output trend in the two groups. This parameter sharply increases in the group of patients with a reduction in TVR (Group B) as a compensation response ensuring a proper peripheral vascular filling. In the Group A we can notice an opposite trend with a progressive reduction in CO values. At 22-23 weeks of gestation there is a statistically significant difference in CO between the two groups (5.45 ± 0.66 vs 7.64 ± 1.44, p < 0, 01).

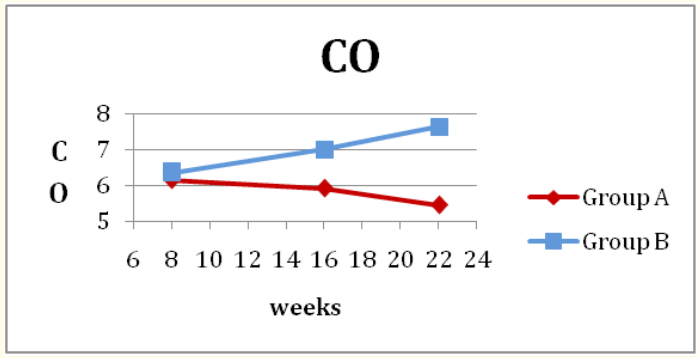

Figure 2: *CO trend between the two groups.*

Figures 3 and 4 shows the trend of stroke volume and heart rate that progressively increase in patients belonging to the Group B. This does not occur in the group A that shows a decrease in both stroke volume and heart rate.

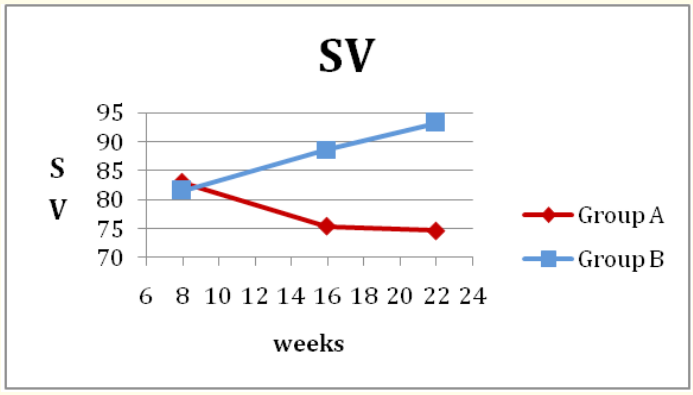

Figure 3: *SV trend between the two groups.*

Both groups show a progressive decline in SBP and DBP even though this is more pronounced and significantly lower in the group of women with low TVR at 22-23 weeks (Figures 5-6).

Discussion

Pregnancy is characterized by important hemodynamic changes in order to promotematernal physiological cardiovascular adaptation. The introduction of USCOM has provided non invasive means for the evaluation of maternal cardiovascular adaptation. The accuracy of the system has been improved through numerous studies in laboratory, compared with other methods and in various clinical applications and has shown in a previous study the mean difference between observers was 0,16 ± 0,59 l/min/m and Lin's concordance correlation coefficient was 0,87 [12].

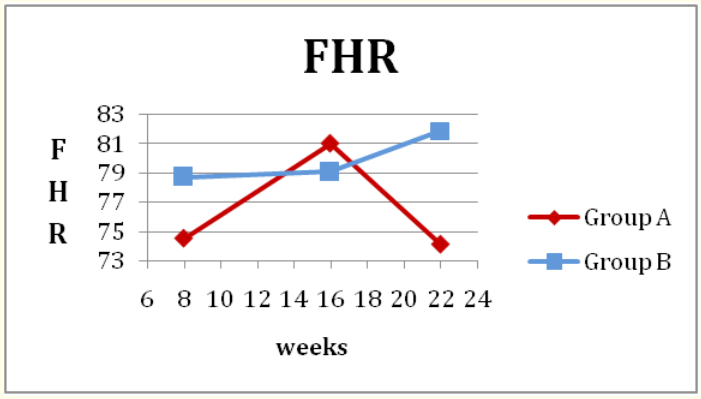

Figure 4: *FHR trend between the two groups.*

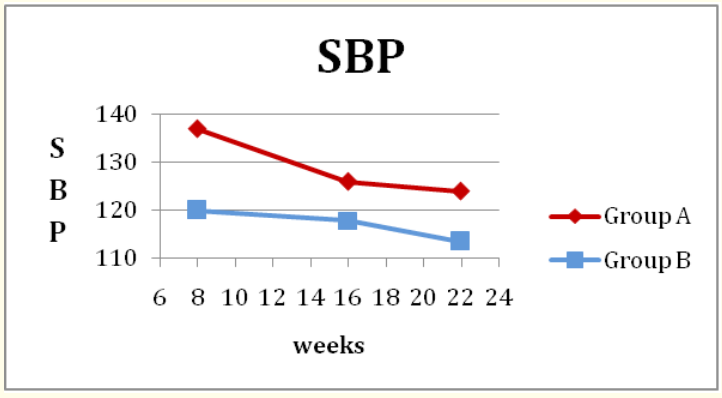

Figure 5: *SBP trend between the two groups.*

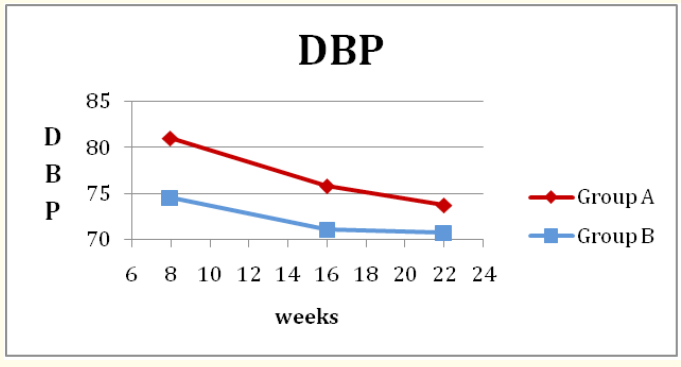

Figure 6: *DBP trend between the two groups.*

This study was designed to understand the evolution of maternal haemodynamics and determine if women at high risk of developing hypertensive complications in pregnancy could be identified prior to the clinical expression of pathological conditions.

The purpose of our study was to evaluate these hemodynamic changes during the first two trimesters of pregnancy. Our data showed that into 37 patients group (26.5% of the total) withpersistently elevated TVR values at 22-23 weeks, 15 women (10% of the total) experienced complications such as gestational hypertension, preeclampsia and intrauterine growth restriction. According to our data, a maternal hemodynamic condition characterized by persistently elevated TVR values (> 1200 dyne/sec/cm^{-5}) in the second trimester of pregnancy probably represents a risk factor for a poor fetal-maternal outcome.

From our results, the risk for developing hypertensive disorders or IUGR in patients with elevated TVR values in the second trimester of pregnancy is 1:25.

Our results show how the study of maternal vascular conditions during the first half of pregnancy is crucial in order to identify significant predictor for the onset of hypertensive disorders, such as gestational hypertension, preeclampsia and intrauterine growth restriction. The knowledge of this maternal condition allowed us to identify a group of so-called low-risk women with total vascular resistance values below 1000 dyne/sec/cm^{-5} that reflects the creation of an adequate low resistance and high capacitance vascular placental bed.

Similarly, high total vascular resistance values could be an early predictor of failure cardiovascular adaptation representing a high-risk group of pregnant women that need to be strictly monitored.

The results of this observational study warrant a more widespread trial to determine the outcomes benefit of a shift from blood pressure screening and blood pressure guided therapy to screening to direct Doppler ultrasound measures of stroke volume, cardiac output and total vascular resistance for prediction of negative outcomes and improved therapeutic guidance.

Conclusions

In conclusion, TVR might help to identify pregnant women at high risk of developing hypertensive complications even before the onset of elevated blood pressure values and clinical expression of pathological conditions.

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