UTERINE ARTERY DOPPLER IN THE ASSESSMENT OF RISK FOR DEVELOPMENT OF PREECLAMPSIA AND INTRAUTERINE GROWTH RESTRICTION

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ABSTRACT:
Objective: To determine the value of color Doppler assessment of the uterine arteries at 19-22weeks of gestation in predicting the subsequent development of pre-eclampsia and fetal growth restriction.
Design: prospective screening study
Setting: university hospital
Patients: one hundred pregnant women (at 19-22 weeks gestation) who attended to El-Minia maternity hospital for routine antenatal care between December 2009 and October 2010
Interventions: the mean pulsatility index (MPI o f both uterine arteries was calculated
Results: statistically significant relation between elevated uterine artery Doppler and adverse pregnancy outcomes especially those occurring earlier in pregnancy course
Conclusion: our results show that a single 19-22 weeks uterine artery Doppler assessment was feasible and useful and is able to detect pregnant women with a high risk for early –onset adverse outcomes that relate to impaired trophoblast invasion in the low and high risk populations

KEY WORDS:
Uterine Artery Doppler
Pre-Eclampsia Intrauterine Growth Restriction

INTRODUCTION:

Preeclampsia is a rise in the blood pressure accompanied by proteinuria, pathological edema, or both in a pregnant woman, who was previously normotensive. Maternal complications of pre-eclampsia include coagulopathy, renal and liver failure, and stroke (J. C. Hauth et al., 2000). Adults who were affected by intrauterine growth restriction in utero are at increased risk for cardiovascular disease, hypertension and type 2 diabetes (A. T. Papageorghiou et al., 2004). Intra-Uterine Growth Restriction, or small for gestational age (SGA) or dysmaturity defined as birth weight less than 10^{th} ercentile for its gestational age. It is about 4% to 8% in developed countries and 6% to 30% in developing countries (Gabbe, 1996). In uncomplicated pregnancies, the spiral arteries undergo a series of changes that convert them from small-diameter, high-resistance vessels into low-resistance non-responsive channels. In some cases there is defective trophoblastic invasion and an inadequate maternal vascular response to placentation, and this is associated with subsequent development of pre-eclampsia and fetal growth restriction. In these pregnancies, the uteroplacental circulation remains in a state of high resistance, which causes generalized endothelial cell injury (Kazım, 2008).

The local production of vasoactive substances, such as prostaglandins, endothelins and nitric oxide, is impaired

and this leads to vasospasm in the small arterioles of the uteroplacental compartment as well as of other systemic vascular beds (Postovit, 2001). Blood flow through the uteroplacental circulation can be studied non-invasively using Doppler ultrasound. The impedance to flow in the uterine arteries decreases with gestation in normal pregnancies, reflecting the trophoblastic invasion of the spiral arteries and their conversion into low-resistance vessels (Papageorghiou, 2005). Preeclampsia and fetal growth restriction (FGR) is major causes of perinatal mortality and morbidity. Both conditions are thought to be the consequence of impaired trophoblastic invasion of the maternal spiral arteries and the physiological reduction in vascular resistance in the uteroplacental circulation (Campbell, 1983). Preeclampsia & IUGR are appropriate diseases to screen, as they are common, important, and increases both maternal mortality and perinatal mortality. However, to date, no test has been shown to appropriately screen for them.

PATIENTS AND METHODS:

The present study included 100 pregnant women (at 19-22 weeks' gestation) who attended to EL-MINEYA maternity hospital for routine antenatal care between December 2009 and October 2010.Patients included in the study had the following criteria: Gestational age 19-22 weeks, Singleton, No previous or current history of any medical disorders. The exclusion criteria included: Gestational age <19 or >22 weeks, multiple pregnancy, Patient having medical disease. The patients were divided into two groups: Group I: Pregnant women with abnormal uterine artery Doppler waveforms (that is, showing bilateral early diastolic notch), Group II: Pregnant women with normal uterine artery Doppler waveforms matched for age, ethnic group. All women gave informed consent before participating in the study.All cases were subjected to through history taking, full general(to exclude medical disorder such as hypertension, diabetes mellitus, anemia, renal troubles, or connective tissue disease) and obstetric examination ((including routine ultrasound scanning) was done to exclude pregnancy abnormalities such as IUGR, oligohydramnios or multiple gestations). All women were subjected to transabdominal assessment of the uterine arteries as follows: Uterine artery Doppler velocimetry was evaluated at 19-22 weeks' gestation by abdominal ultrasound using TOSHIBA COLOUR DOPPLER 3.5 MHz at each Examination the patient was in a semi recumbent position with her head and chest supported at approximately 45^{O} to the Horizontal. The technique of uterine artery Doppler: The Doppler velocimetry measurements of the uterine artery are taken at the point just distally to the crossover with the iliac artery, before uterine artery division into arcuate arteries**.** The process was then repeated for the contralateral uterine artery and the mean PI (MPI two vessels were calculated.

The studied group was then classified into two subgroups:

Women with normal (MPI of uterine arteries and no early diastolic notch noted, women with elevated (MPI and or with early diastolic notches. (Screen positive group).

The screen positive group was then strictly followed up till delivery in the high risk clinic weekly by blood pressure measurement, urine analysis for proteinurea, ultrasound scanning using growth charts (for early detection of IUGR). While the other group received the routine antenatal care.

Information about the course of pregnancy was recorded, including gestation age, mode of delivery and infant birth- weight for all women.

Preeclampsia is defined in accordance with criteria of the interna-

tional society for the study of hypertension in pregnancy i.e., hypertension (one diastolic blood pressure reading > 110mmHg or two consecutive diastolic blood pressure readings > 90mmHg at least 4 hours apart in combination with proteinuria (> 300mg total protein in a 24 hours urine collection or, if this was not available, +2 protetinuria by dipstick on two consecutive occasions at least 4 hours apart).

Statistical methodology:

Fisher's exact test was used to analyze maternal history variables and independent *t*-test—Mann-Whitney *U* test—was used for continuous variables analysis where appropriate.

The sensitivity (S), specificity (E), positive predictive value (PPV), negative predictive value (NPV), and likelihood ratio (LR) for a cut-off mean PI of 1.66 (95^{th} centile) and for a mean PI of 1.40 (90^{th} centile) and presence of bilateral notches in the prediction of preeclampsia and/or IUGR were calculated. Differences were considered significant when $P < .05$.

Logistic regression was used to obtain the odds ratio (OR) and 95% CI for PE in relation to maternal history variables. A multivariate analysis to draw the receiver-operating characteristics curves (ROC) was performed using maternal history variables found to be independent in a univariate analysis.

Data was analyzed using SPSS 13.0 (SPSS, Chicago, Ill, USA) and STATA/SE 8.2 statistical packages.Data was collected, tabulated, coded then analyzed using SPSS computer software version 12.

RESULTS:

In the group of women who subsequently developed PE/IUGR, MPI was higher than in those who did not develop any complication (median 1.25(0.60) versus 0.82 (0.25), P < 0.001). The highest values of MPI were among patients that developed early-onset disease (median 1.45 (0.35) versus 1.21(0.35), P < 0.01). Overall, PE occurred in 5 cases (5%), early-onset PE in 2 cases (2%), IUGR in 5cases (5%); early-onset IUGR in 3 cases (3%) and early-onset PE with IUGR in 7 cases (7%).

Table (1): Comparison between cases and controls as regard general data

Variables	Cases N=11 Mean ± SD	Controls N=89 Mean ± SD	T	P
Age	23 + 4.2	21.8 + 3	1.9	>0.05
Gestational Age at delivery	36.8 ± 1.7	38.6 ± 1	1.8	>0.05
BMI	29 ± 2.9	30.3 ± 3	1.7	>0.05

This table shows no statistically significant difference could be detected between both groups as regard general data by using unpaired t-test and chi-square test.

Table (2): Comparison between cases and controls as regard clinical data

Variables	Cases N=11 Mean ± SD	Controls N=89 Mean ± SD	T	P
SBP	158 ± 12.8	112 ± 11	20	<**0.01
DBP	96.4 ± 4.8	75 ± 6.1	19	<**0.01
Heart rate	94 ± 5.2	84 ± 6.5	8	<**0.01

Significant statistical difference was found between cases & controls as regarding clinical data

Table (3): Comparison between cases and controls as regard mode of delivers

Variables	Cases N=11	Controls N=89	X^2	P
SVD	(%54)	(%82)	11	<**0.01
CS	(% 46)	(%18)		

Highly significant test p<0.01

Table (4): Comparison between cases and controls as regard fetal weight

Variables	Cases N=11	Controls N=89	X^2	P
Mean ± SD	1450+-294	3079 ± 345	10	<**0.01
Range	1200-2000	2500 - 3800		

Highly significant test p<0.01

Table (5): Frequency of adverse pregnancy outcome as regarding PE, IUGR & abruption among the studied population.

	Total = 100	
	No	**%**
Normal	89	89%
Early PE	2	2%
Late PE	3	3%
IUGR	5	5%
Abruption before 30 weeks	1	1%

Only 11% of cases had pregnancy complications

Table (6): Frequency of early diastolic notches among the studied population.

	Total = 100	
	No	**%**
Yes	17	17%
No	83	83%

17% of cases had early diastolic notch while 11% of cases showed pregnancy complications i.e. 6% of cases who had early diastolic notches were normal throughout pregnancy.

Table (7): Screening characteristics for MEAN PI > 1.04 irrespective of early diastolic notches for prediction of PE, IUGR

	Sensitivity	Specificity	PPV	NPV
PE	80%	82.1%	19.04%	98.7%
Early PE	90%	81.4%	13.8%	98.7%
Late PE	70.6%	80.6%	9.5%	95.7%
IUGR	80.6%	83.1%	23.8%	98.2%

Table (8): Screening characteristics for mean PI > 1.04 when combined with early diastolic notches.

	Sensitivity	Specificity	PPV	NPV
PE	80.3%	93.6%	14.2%	95.6%
Early PE	89.9%	92.7%	0%	96.7%
Late PE	70.1%	93.8%	14.2%	98.9%
IUGR	82%	94.7%	28.5%	96.7%

False positive results=11% in all patients

Table (9): Comparison between uterine PI versus other variables among the studied cases

Variables	PI	
	R	P
Age	0.25	> 0.05
Age at delivery	0.19-	> 0.05
BMI	0.16-	> 0.05
Fetal weight	0.66	<**0.01
SBP	0.67	<**0.01
DBP	0.48	<**0.01
Maternal heart rate	0.60	<**0.01

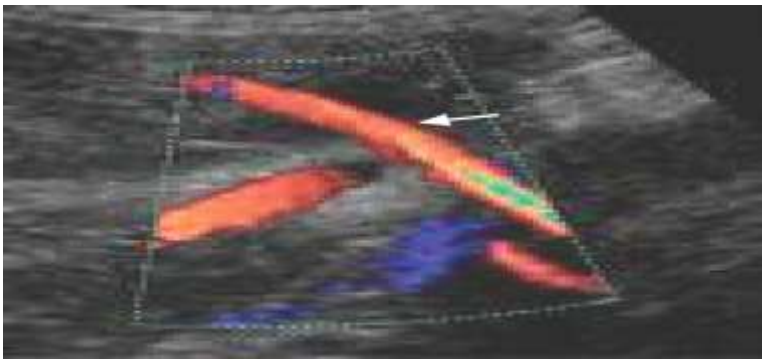

Figure (1): Colour Doppler ultrasound scan showing uterine artery (arrow).

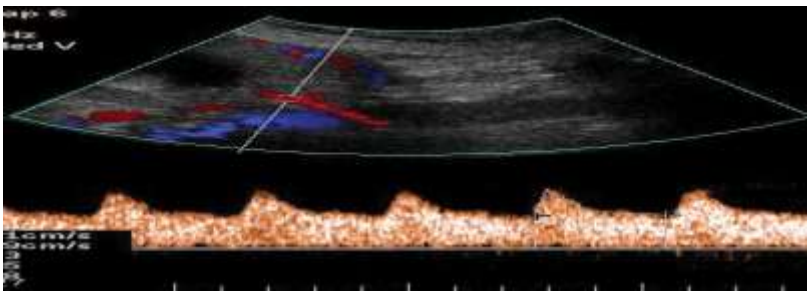

Figure (2): Uterine artery Doppler ultrasound scan showing normal waveform.

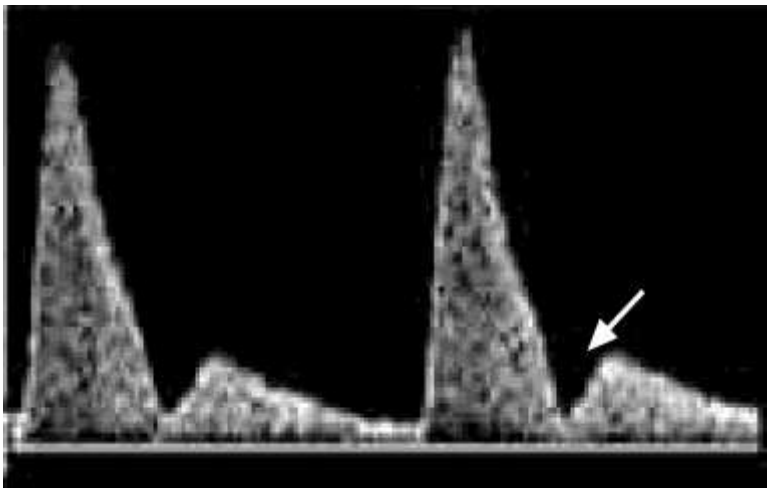

Figure (3): Uterine artery Doppler ultrasound scan showing early diastolic notch (arrow). The presence of diastolic notches is associated with an increased risk of pre-eclampsia and intrauterine growth restriction.

Figure (4): Abnormal uterine artery Doppler wave form demonstrating high resistance.

DISCUSSION:

In our screening program we have used the uterine artery as the study vessel and used the mPI as the study paramter like that done by (Aris T Papageorghiou et al., 2005).

We have used color Doppler for obtaining wave forms of the uterine arteries. Color flow imaging was found to allow a higher number of reliable recordings to be obtained, to shorten the observation time, and to reduce the intra-

and interobserver coefficients of variation Maulik, Yarlagadda, Downing, 1990.

Our findings have shown that measurement of the uterine artery MPI at 19-22 weeks gestation can identify 90% of pregnancies that will subsequently develop early-onset PE and 80.3% of pregnancies that develop early-onset IUGR, with a 12% false-positive rate.

In our screening program, the gestational age was moved to 19–22 weeks, which is when the routine abnormality scan is normally performed in most countries (Papageorghiou et al., 2001).

Although a two-stage screening program has been recommended due to a higher false-positive rate around 20 weeks of gestation, we have found that, for the same false-positive rate, a one-stage screening test at 20 weeks gestation has a similar detection rate for PE or IUGR to studies performed at 22–24 weeks gestation (Bower et al., 2000).

We have also determined that with the same false-positive rate (11%), uterine Doppler MPI gave similar results to bilateral notches and MPI, so the addition of bilateral notches did nothing to improve screening characteristics. Moreover, the use of the PI has removed any subjectivity associated with the definition and interpretation of the presence of notches in the waveform (Papageorghiou et al., 2005).

Early diastolic notches can be a physiologic finding till 24-26 weeks' gestation. The prevalence of bilateral diastolic notches at 18-22 weeks is more than 10% Papageorghiou et al., 2002 so we have excluded the reliability of the notch from our study.

While other studies like that done by Harrington et al., 2003 has stressed the role of persistent early diastolic notch as predictor of adverse pregnancy outcome. We have considered early-onset PE and IUGR as different outcomes from those conditions that were diagnosed near to term (Harrington, 1996).

Previous studies have established that uterine Doppler is much better at identifying the more severe early-onset cases (Albaiges et al., 2000 & Papageorghiou, 2005).

In our study the sensitivity of uterine artery Doppler for early onset pre-eclampsia was 90% while for late PE it was only 70%.

It has also been demonstrated that uterine Doppler screening is better in predicting severe early-onset disease or PE associated with IUGR, with sensitivities of 80 to 90% (Papageorghiou, 2001).

The classification of PE &IUGR at or near term has clinical importance since early-onset PE is commonly associated with IUGR, abnormal uterine Doppler, and adverse maternal and neonatal outcomes (Sibai, 2005, Murphy 2000 & Ness, 2006).

Our results are in agreement with the results of the Arduini D. et al., (1991) no evident differences were found in arteries (uterine, arcuate or trophoblastic) between patients with later complications and those with normal pregnancy, Antsaklis A. et al., (2000) concluded that normal uterine artery Doppler FVWs in early pregnancy allowed to distinguish the group of pregnancies with very low risk to develop pregnancy vascular complications, Chien PF et al., (2000) found a significant association between uterine artery PI values (comparing lowest and highest quartile) at 12-13 weeks and hypertensive disorders (RR=4) & Harrington K. et al., (1997) values from women with a normal pregnancy outcome, differ significantly from women who subsequently developed

PPIH (mean RI = 0.80 vs.. 0.695, p < 0.001).

Aquilina J. et al., (2000) examined 614 primiparous women by color flow/pulse Doppler imaging of both uterine arteries at 20 weeks gestation. Receiver operator characteristic (ROC) curves were created for the A/B ratio, RI and A/C ratio for placental and non-placental uterine arteries, individually or in combination with the presence of unilateral or bilateral notches. The highest sensitivity (88%) and specificity of (83%) was obtained using bilateral notches/mean RI > 0.55(50^{th} centile) and unilateral notches/mean RI > 0.65 (80^{th} centile), when the false-positive rate was set at 17%. Placental velocimetric indices performed better than mean indices but the differences in sensitivity at the set false-positive rates were not statistically significant.

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دوبلر الشريان الرحمي في تقييم مخاطر حدوث تسمم الحمل وتأخر النمو الجنيني

مقدمه:
يعد تسمم الحمل وتأخر النمو الجنيني من أهم المخاطر التي تهدد الأم والجنين وقد تؤدي إلي إنهاء مبكر للحمل.
ويعتبر من أهم أهداف طب الأم والجنين اكتشاف الحالات الخطرة في عمر مبكر نسبيا من الحمل لتحديد التدخل الملائم لكل حاله بهدف تحسين ناتج الحمل.
ويرتبط تسمم الحمل وتأخر النمو الجنيني بقصور الدورة الدموية بين المشيمة وبطانة الرحم والتي يمكن دراستها بطريقه لا تدخليه بواسطة موجات الدوبلر.
وخلال الخمس وعشرين عاما الفائتة تم إجراء العديد من الدراسات والتي أكدت جميعها صحة الملاحظة الاوليه وهي أن تسمم الحمل.
وتأخر النمو الجنيني كلاهما مرتبط بزياده المقاومه لمرور الدم في الاوعيه بين المشيمة وبطانة الرحم ولكن هذه الدراسات اختلفت في طرق البحث وإحصاء الناتج.
الهدف من الدراسة:
تحديد أهميه دوبلر الشريان الرحمي في عمر 19-22 أسبوع من الحمل في توقع حدوث تسمم الحمل وتأخر النمو الجنيني.
المواد المستخدمة وطرق البحث:
شملت هذه الدراسة مئة سيده حامل من اللاتي أتين لمتابعه الحمل الروتينية في مستشفي سوزان مبارك الجامعي في الفترة من مارس 2010 حتي اكتوبر2010.
وكانت خطه العمل كالتالي:
1 -ان يكون عمر الحمل عند إجراء الفحص 19-22اسبوع.
2- أن تكون السيدة حامل في جنين واحد طبيعي.
3- -ليس لديهن أي تاريخ أسرى لأمراض قصور الدم المختلفة.
ويستثني من تلك الدراسة من لديهن أي تاريخ مرضي ايجابي سابق أو عيوب خلقيه أو حمل توأمي .
وكنت خطه الدراسة قائمة علي إجراء فحص بواسطة موجات الدوبلر للشريان الرحمي في الفترة من 19-22 أسبوع من الحمل ويتم تقسيم السيدات بناء علي هذا الفحص إلي مجموعتين:
1- السيدات اللاتي تعانين من ارتفاع في قياسات نسبة تدفق الدم بالشريان الرحمي
2- السيدات اللاتي لديهن قياسات طبيعة لنسبة تدفق الدم بالشريان الرحمي
تم قياس ضغط الدم وتسجيله، ومتابعة دقيقة للأم حتى الولادة.
النتائج:
تم رصد النتائج وتحليلها إحصائيا
ً النتائج و المناقشة:
قد أسفرت هذه الدراسة عن وجود علاقة ملحوظة ذات دلالة احصائيه بين ارتفاع قياسات نسبة تدفق الدم بالشريان الرحمي في المجموعة الأولي وحدوث تسمم الحمل وتأخر النمو الجنيني بينما وجدت علاقة عكسية في المجموعة الثانية في السيدات.
لقد ثبت بالعديد من الدراسات ارتباط ارتفاع قياسات نسبة تدفق الدم بالشريان الرحمي وحدوث مضاعفات الحمل الناتجة عن غزو الطبقة الأرومية غير الكامل لبطانة الرحم
والذي يمكن من خلاله التنبؤ بحدوث مثل هذه الأمراض قبل ظهورها .
وخلصت الدراسة إلي أن فحص الشريان الرحمي بواسطة موجات الدوبلر من الممكن استخدامه كفحص للتنبؤ بحدوث مضاعفات تسمم الحمل وتأخر النمو الجنيني ويمكن علي أساسه تحديد مستوي متابعه الحمل التي تحتاجها بهدف تحسين صحة الأم والجنين.