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Uterine Doppler Pulsatility Index in Prediction of Pre-eclampsia

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Abstract: ***In 2017, 810 women died every day due to pregnancy complications which composite preeclampsia, postpartum bleeding, infection, unsafe abortion and other delivery complication, 90 percent of which occurred in developing country. Preeclampsia with a case Fatality Rate of 6.4 merit considerable measures for prior anticipation and early detection to decline the maternal mortality rate. Knowing the pathophysiology of the disease, many tests have been introduced with various sensitivity and specificity. With the ever growing imaging technology, Doppler ultrasound may become a milestone for prediction of preeclampsia in second trimester. Objective: This study aims to look for evidence on the sensitivity of uterine Doppler pulsatility index (Ut-PI) either individually or in composition with other parameters in anticipation of PE. Methodology: This study quested for literature entailing the sensitivity of Ut-PI in preeclampsia prediction with highest observations. Conclusion: It is strongly suggested that combination of Ut-PI significantly promote the accuracy of PE anticipation. Integration of Ut-PI with PAPP-A and PP13 foresee the preeclampsia with a sensitivity of 92.63***

Keywords: preeclampsia, uterine Doppler pulsatility Index, PAPP-A, PP13, Placenta size, PLGF

1. Introduction

Preeclampsia is a fatal complication of pregnancy affecting 2-8% of pregnant women. According to Sibai and colleagues mortality rate in severe cases are 135/1000 pregnancies [1]. Preeclampsia (PE) is defined as hypertension later than 20 weeks of gestation coexisting with proteinuria more than 300mg/24hr or +1 on dipstick test whereas eclampsia (Ec) is the presence of grandmal seizures along with severe preeclampsia [2].

Although the exact pathophysiology of PE is unknown, it is presumed that failure of Syncytotrophoblasts to invade dilated uterine spiral arteries in second trimester leads to IUGR and preeclampsia at various level [3]. This process starts in early pregnancy and extends to the myometrial course of spiral arteries by the middle of second trimester. These changes are reflected in the uterine artery Doppler waveforms. Defective remodeling process then leads in to subsequent development of preeclampsia and fetal growth restriction. With the state-of-the-art knowledge, extensive research has been done to predict occurrence of preeclampsia through testing biomarkers (chemical and physical) in the earliest possible stages of pregnancy. Uterine artery velocimetry, maternal blood pressure, roll-over test and transcranial Doppler velocimetry are the biophysical determinants and number of maternal and fetal biochemical markers are claimed to foresee preeclampsia (table 1.1) [4].

Table 1.1: Predictive tests for anticipation of preeclampsia

Fetal-placental unit dysfunction tests	Beta HCG
	Alpha fetoprotein
	Inhibin A
	Pregnancy Associated Plasma Protein A
	Activin A
	Disintegrin and metalloproteinase 13
	Placenta Protein 13
Utero-placental perfusion criteria	Uterine artery Doppler pulsatility index
	Roll over test, isometric test, angiotensin sensitivity test
	Transcranial Doppler velocimetry
Renal dysfunction related tests	Uric acid
	Urinary Kallikerein
	Microalbuminuria
	Podocyteuria
	Urinary calcium excretion
Endothelial dysfunction and oxidant related tests	Fibronectin
	Endothelial cell adhesion molecules
	Homocysteine
	Circulating Angiogenic Factors
Other tests	Cell free fetal DNA
	Proteomic, metabolomics and transcriptomic markers

Each of these tests shows varying sensitivity and specificity which makes some of them more plausible than the others. Moreover; combined tests have also been used to yield better prediction in preeclampsia development. It has been asserted that a comprehensive screening test which entails maternal factors, biophysical and biochemical markers can predict 90% of women who will develop early preeclampsia [17].

2. Uterine Artery Doppler Waveform

The uterine artery Doppler waveform in early pregnancy shows a rapid acceleration and deceleration of the flow velocity during systole, then in the early diastole a deceleration, known as the diastolic notch, is followed by a slight rise. Factors that influence the waveform include gestational age, maternal heart rate, location of placenta and uterine artery system [5].

The pulsatility of the waveform shows a downward trend at the beginning of pregnancy, more rapidly until 14 and 16

weeks of pregnancy than the declining rate thereafter until 26 gestational age. It shows a constant rate in the remaining time of pregnancy [6]. A continuous decline until 34 weeks is claimed in a recent study, however. [7].These changes reflect profound decline in the utero-placental circulatory impedance during early pregnancy, consequent to the dramatic transformation of the spiral endometrial arteries, with the invasion of the specialized trophoblastic cells. Uterine artery waveforms in the same side of placenta show a lower pulsatility than those from the contralateral location [8]. Maternal heart rate on the diastolic run-off time influences the waveform and its pulsatility. A higher rate will shorten the diastolic runoff time, thereby decreasing the pulsatility and vice versa.

Thus, Doppler waveforms from the spiral arteries show significantly lower pulsatility than those from the main artery, reflecting progressive decline in the circulatory impedance down the arterial tree.

This paper investigates the magnitude of Uterine Doppler PI and its combination with other biomedical indicators in anticipation of preeclampsia.

3. Transformation of Uterine Artery Doppler throughout of pregnancy

Uterine pulsatility index continues to fall during span of pregnancy [7]. Heart rate of mother, use of medication for high blood pressure, and hormonal changes in the menstrual cycle, and chronic hyperandrogenism in the polycystic ovarian syndrome can influence the resistance in uterine artery. Moreover ethnicity and high BMI are indicators of Ut-PI. Reference range for uterine pulsatility index from 11-14 up to 41 weeks of gestation has been published by researches. The pulsatility index or resistance index is high in the upper parts of utero-placentation circulation since the resistance is distributed upstream. Fall in impedance in uterine vessels following trophoblastic invasion leads to decline in uterine artery PI and RI values with increasing gestational age. The low sensitivity of Ut-PI escalates considerably from 34-76% by 90 % when is performed along with biomedical markers in multi-parametric models [10].

4. Uterine Doppler Pulsatility Index combination with Placenta Protein 13 (PP-13) and pregnancy associated plasma protein A (PAPP-A)

PAPP-A is an insulin like growth factor which binds with protein protease and facilitates the invasion of trophoblasts whereas PP13 binds with protein of extracellular matrix between placenta and myometrium and contributes in implementation and remodeling of placenta. Decreased level of both of these biomarkers in the first trimester may warn development of preeclampsia later in pregnancy [10].

A study conducted by Ghada Abdel Fattah Abdel Moety et al in 2015 on 100 pregnant women in 11-14weeks gestational age examined Ut-PI, B-HCG and PAPP-A. Uterine PI, being the most accurate biomarker in prediction of preeclampsia, yields results with remarkable highest sensitivity (100%) its specificity raised from 56% to 94.44% when is combined with PAPP-A [11].

Similarly in another study performed by Di Lorenzo et al in 2012 on 2118 expectant women who underwent an laneuploidy screening claims that however Uterine PI does not improve the prediction rate, its combination with PLGF, on the other hand, shows 60% sensitivity[12].

A case control study carried out by Spencer et al in Harold Wood Hospital in 2007 proved that amalgamation of first trimester PP 13 and PAPP-A biomarker with uterine Doppler in second trimester foresee the probability of development of Preeclampsia with sensitivity of 74% and 76% , respectively. With individual sensitivities of 44% and 24%, former for PP 13 and later for PAPP-A, it preemptively depicts the contribution of Ut-PI in the increase of their accuracy in the prediction of PE. However, the main downside of Ut-PI is its late favorable diagnostic period [13].

5. Uterine Doppler Pulsatility Index combination with placental volume

Considering the underlying poor invasion of trophoblasts in preeclampsia, it coexists with the low volume of placenta in the first trimester of pregnancy. Owing to recent breakthroughs in the field of ultrasonic imaging and introduction of 3D and 4D technologies placental size can be measured [14].

Gedilkabasi et al concluded from a prospective study combining Ut-PI with placental volume and PAPP-A in 2016, that despite all of these tests had shown almost equal sensitivity in prediction of preeclampsia, this sensitivity promotes whenever an abnormal Ut-PI is combined with either of tests. The sensitivity of the Ut-PIwas found to be 70.73% that impressively raised to 92.68 % when was annexed with each of the mentioned parameters [15].

Giuseppe et al discovered from a prospective study in 2007 on 348 nulliparous pregnant women via transabdominal uterine artery flow velocimetry and pulsatility Index, that however there is no relationship between placental size and uterine artery pulsatility index, using these tests together increases the sensitivity of prediction of preeclampsia by 66.7% and delivery prior 32 weeks gestations due to preeclampsia by 83.3% [16].

6. Conclusion

Despite application of Ut-PI is limited to late second trimester period and the skilled technicians and machinery are needed to diagnose abnormality accurately, it has the highest sensitivity amongst other pregnancy parameters and the detection rate for preeclampsia remarkably increases when it is combined with either biomedical marker in the first trimester or ultrasound findings in placental size irregularities. Anticipation of developing preeclampsia is better enhanced when biomarkers (PAPP-A and PP13) are used with uterine Doppler pulsatility index compared with

ultrasonic placental size measurement.

The dire outcome of preeclampsia mandates health systems to devise screening procedure with higher efficiency and availability in order to initiate a reduction of death related to hypertensive disorders in pregnancy.

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