

**Ph. D. THESIS**

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**THE ROLE OF DOPPLER SONOGRAPHY IN THE DETECTION OF  
DYSFUNCTIONAL PLACENTAL PERFORMANCE AND FETAL  
HYPOXIC RISK**

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**The role of Doppler sonography in the detection of dysfunctional placental  
performance and fetal hypoxic risk**

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## **I. INTRODUCTION, OBJECTIVES**

Doppler sonography has become a part of routine antenatal surveillance in obstetrics during the past decade. Blood flow measurement has significant impact in the detection of placental and fetal dysfunction since the haemodynamic changes in the uteroplacental and fetal vessels can be demonstrated well before the clinical manifestation of obstetric complications.

In the majority of the Hungarian obstetric departments, Doppler ultrasound equipment is primarily used for anatomical screening and biophysical profile assay. Blood flow measurement in the uteroplacental vessels in order to screen for high risk pregnancies has not become a routine practice yet. Consequently the introduction of a Doppler screening method to distinguish low and high risk pregnancies is desirable.

Fetal monitoring is based on a diagnostic procedure, among which Doppler sonography has become a top-level non-invasive method. Despite the accuracy of these tests, perinatal morbidity and mortality is frequently associated with intrauterine hypoxic stress. Every fourth case of cerebral palsy is caused by intrauterine events before the onset of labor. Doppler ultrasound is capable to detect beginning haemodynamic alterations, therefore the method can be utilized in the early detection of maternal and fetal complications. Recently published meta-analysis has proved that systematic application of Doppler sonography has resulted in a 50% reduction of perinatal mortality among high-risk pregnancies.

The aim of my thesis is to clarify the proper role of Doppler ultrasound in the recognition of placental dysfunction and fetal hypoxic risk on the basis of the scientific literature and the experience gained in the Department of Obstetrics and Gynecology of the Medical University in Debrecen.

I intended to:

1. describe the salient methodological aspects of Doppler ultrasound in order to facilitate consistent practical application in obstetrics, additionally to introduce the analysis of blood flow velocity waveforms, the numerical indices describing the waveforms, along with the practical aspects of flow measurement in the uterine and fetal arteries and veins.
2. analyze the pathophysiological background of normal and defective implantation. I was also searching for clinical data supporting the proposal of introducing Doppler sonography as a functional screening test during the second and third trimester gestation performed as the blood flow velocimetry of the uterine and the umbilical arteries.
3. distinguish if the uterine artery Doppler measurement can improve the clinical diagnosis of pathologic pregnancies. I analyzed the main perinatal results of high-risk pregnancies complicated with proteinuric hypertension and fetal growth retardation where unilateral and bilateral uterine artery „notching” was detected during the third trimester of gestation.
4. analyze the haemodynamic characteristics of the fetal and umbilical arterial circulation during the third trimester of uncomplicated pregnancies. I aimed to establish reference ranges of the Resistance Index and the Pulsatility Index of the umbilical artery, the fetal descending aorta and the middle cerebral artery in order to facilitate the uniform application of the Doppler ultrasound examination in obstetrics.
5. summarize the physiologic and practical background of Doppler ultrasound assay of the fetal central venous circulation along with clinical indications and typical clinical examples of the velocimetry of the ductus venosus, inferior vena cava and the umbilical vein.
6. introduce the effects of chronic and acute hypoxia on fetal hemodynamics. I also planned to present guidelines for the indications and systematic application of fetal Doppler examinations during the third trimester of gestation.

7. examine if the physiologic fetal arterial blood distribution can be expressed by the ratio of the haemodynamic resistance between the descending aorta and the cerebral arteries during the third trimester of gestation. In addition, to examine if Doppler index ratios can be utilized to improve fetal monitoring.
8. explore the perinatal results of those pregnant women, in which the fetal arterial redistribution was indicated by the increased aortic-cerebral ratio.

## **II. PATIENTS, METHODS**

We carried out our examinations in the Ultrasound Laboratory by the color-Doppler ultrasound equipment ATL HDI-3000 (Advanced Technology Laboratories, Bothen Washington) on pregnant women cared by the pregnancy clinic and the pathologic pregnancy ward of our department. The main indication for blood flow measurement was non-reassuring non-stress test, decreased biophysical profile, pregnancy-induced hypertension, fetal growth restriction and twins or multiple twins.

We analyzed the Doppler results of 200 uncomplicated gestations, 100 pregnancies with fetal growth retardation, and 100 with abnormal Doppler indices along with 50 twins and multiple twins. Altogether we examined 500 fetuses between the 27<sup>th</sup> and 42<sup>nd</sup> gestational weeks and performed an average of three Doppler examinations per fetus. Approximately 18.000 data were collected prospectively, completed by postnatal results. We performed a retrospective data analysis. Postnatal results include gestational weeks, birth weight, the method of delivery, documented subnatal hypoxic event, gender of the newborn, the Apgar scores of 1, 5, 10 minutes and occasionally, the cord blood pH values along with eventual neonatal complications.

Gestational ages were calculated from the last normal menstrual period, and confirmed by the crown-rump-length values obtained from the first trimester (8-12 weeks) and third trimester (30-32 weeks) ultrasound report. The reference ranges of Doppler indices were established on the basis of the Doppler results of pregnant women without symptoms and complications who delivered vaginally between the 37<sup>th</sup> and 41<sup>st</sup> week, with no documented signs of fetal hypoxic event during labor. Newborns did not need neonatal intensive care and there were no chromosomal abnormalities or major malformations.

In our investigation, the pulsed wave ultrasound signals were recorded by a 3.5-5 MHz curvilinear transducer. Doppler velocity waveforms were obtained from the umbilical artery, left and right uterine arteries along with the fetal descending aorta and the middle cerebral artery according to the established method of our laboratory similar to the published procedures. Doppler indices (Resistance and Pulsatility Index) were automatically calculated by the software of the equipment.

Data and perinatal results were recorded with the Microsoft Windows Excel program. Mean values and standard deviation were calculated by Statistica for Windows. For evaluating the tendency of haemodynamic impedance in the fetal arteries during the third trimester of gestation, ANOVA analysis of variance and LSD test were applied. Abnormal Doppler indices were compared to the weekly reference values by the Mann-Whitney U test. We applied two variable T test confirmed by the Wilcoxon test to relate the parametric data for evaluating the perinatal outcome. We compared the non-parametric results with the help of the chi-square test. We considered the differences statistically significant at a p value <0.05.

### **III. COMMENT ON THE RESULTS, CONCLUSIONS**

We systematically summarized the clinical experience gained at the Ultrasound Laboratory of the Department of Obstetrics and Gynecology. We proposed practical guidelines for Doppler evaluation of the uteroplacental and the fetal arterial and venous circulation. Summary of the blood flow velocity waveform analysis, and the steps of useful application support consistent clinical comprehension and proper diagnosis.

Defected implantation may be recognized by the Doppler evaluation of the uterine arteries, impaired placental function is reflected by the umbilical blood flow velocity waveforms, while the fetal well being can be described by the simultaneous examination of the descending aorta and the cerebral circulation. When cardiac failure is impending, the qualification of central venous blood flow is inevitable. Obstetric Doppler velocimetry necessitates the computed analysis of flow patterns, along with the quantitative description of Doppler results by the Resistance and Pulsatility indices. The introduction and the clinical application of the reference values provides appropriate interpretation of the physiologic fetal blood flow patterns which is the prerequisite of the diagnostic accuracy of the Doppler ultrasound in obstetrics.

2. The indications of Doppler sonography in obstetrics has been continuously growing. Velocimetry of the uterine and umbilical arteries has practically no disadvantages, contraindications, risks nor excess costs. The screening takes a short time, the procedure is reproducible, providing useful functional information which is consistently comprehensive among obstetricians. Abnormal velocity waveforms obtained from the uterine and umbilical arteries at the 18<sup>th</sup> and 32<sup>nd</sup> weeks of gestation respectively may have significance in predicting adverse perinatal outcome of the pregnancy. Initializing preventive and therapeutic

measures will result in the significant reduction of maternal and fetal morbidity and mortality. The screening test of uteroplacental circulation is a useful method of distinguishing normal and high risk pregnancies.

In order to improve the efficacy of antenatal care, we propose the screening of the uterine circulation at the 18<sup>th</sup> week and the umbilical artery velocimetry at the 32<sup>nd</sup> week of gestation for the early detection of high risk pregnancies complicated by impaired placental function.

3. The unilateral uterine artery notch is associated with increased perinatal morbidity, while the bilateral uterine artery notch is advising the exceptionally high fetal perinatal risk among third trimester pregnancies complicated by preeclampsia or fetal growth retardation. According to the presented clinical implications of the abnormal uterine artery velocity waveforms, alert antenatal and subnatal surveillance of the mother and the fetus (multidisciplinary consultation, medical therapy, stimulation of fetal lung maturation) is recommended in order to avoid or to lessen the expectable complications.

The waveform analysis of the uterine arteries, including the detection of early diastolic notch among high-risk pregnancies, may be considered not only as an additional diagnostic modality, but ultimately also a predictor of the likelihood of perinatal complications, indicating the severity of the adverse outcome. We propose uterine artery Doppler velocimetry to be a routine diagnostic tool for patients suffering from pregnancy induced hypertension or fetal growth retardation.

4. The physiologic blood flow patterns of the fetal and umbilical arteries are represented by the normal values of the Doppler indices. The results of ultrasound velocimetry have significant impact on the method of antenatal care, therefore the knowledge and application of reference values is highly important. The application of normal values in the clinical practice



provides the possibility of consistent understanding. Consequently it is fundamental for the recognition of early stage fetal hypoxic compromise.

During our study we established the reference values of Doppler indices in the fetal descending aorta, middle cerebral artery and in the umbilical artery which is a prerequisite for the ultrasound diagnosis of fetal hypoxic jeopardy.

5. Doppler ultrasonography has given insight to the fetal hemodynamics. The physiologic properties of the fetal central venous blood flow have been recently studied and documented. The abnormal patterns indicate the impaired central venous circulation and the decreased cardiac performance. The characteristic alterations of the venous blood flow velocity waveforms have an important impact in the diagnosis of various pathologic fetal conditions.

We presented the first review in Hungary concerning the available information on the physiology of the fetal central venous circulation and the clinical application of venous Doppler ultrasound examination. The measurement of the fetal venous blood flow will soon become a valuable tool in the management of high-risk pregnancies, which will improve the efficacy of the prenatal care.

6. Doppler sonography provides insight into the uteroplacental and fetal arterial, venous circulation non-invasively. It has a key role in the detection of hypoxic risk since abnormal blood flow patterns can be demonstrated before the clinical manifestation of fetal disorder. Doppler velocimetry facilitates judgment in the obstetric diagnosis, monitoring fetal well-being during pregnancy and labor, scheduling antenatal tests and timing delivery. Recent studies on the effects of chronic and acute hypoxia on fetal hemodynamics have

proved that the early, intermediate and late phases of fetal adaptation can be documented by examining the haemodynamics in different fetal vascular beds.

On the basis of the present knowledge and our experience, we provide a detailed summary about the general and obstetric indications of Doppler velocimetry in the third trimester of gestation. Our proposal for the systematic schedule of Doppler examinations as a part of the antenatal fetal surveillance is also a priority in the Hungarian literature.

7. Doppler ultrasound is used in obstetrics to discover the initial stage of fetal haemodynamic pathology. As a response of hypoxia, the fetal cardiac output is readjusted. Fetal hypoxia decreases the vascular resistance in the cerebral vessels, while the resistance in the aorta increases in correlation with the peripheral vasoconstriction in the splanchnic and skeletal region. Comparing the impedance to blood flow in different vascular areas may improve early recognition of the fetal cardiovascular compensation. Doppler index ratios are more sensitive than independent evaluation of the vessels since they are expressing opposite trends within the normal ranges. We supposed that the normal ranges for the Doppler index ratios, reflecting the physiologic blood distribution may facilitate the recognition the circulatory readjustment. The purpose of the obstetrical Doppler measurement is the proper assessment of the actual fetal condition independent from the placental vascular impedance and the gestational weeks. In our study we constructed reference limits for the aortic-cerebral resistance index ratio between the 28<sup>th</sup> and 41<sup>st</sup> weeks of normal gestation and also presented a cut-off value below which the arterial blood distribution is considered to be physiologic.

We observed that the haemodynamic impedance of the fetal descending aorta and middle cerebral artery are identical and their ratio remains constant during the third trimester of uncomplicated pregnancies. We introduced the aortic-cerebral ratio as a novel approach

into the obstetric practice in Hungary. Application of the ratio offers straightforward interpretation of the fetal arterial blood flow distribution.

8. Abnormal Doppler index ratios facilitate the recognition of pathologic fetal haemodynamic status and the timing of when the hypoxia developed. The pathophysiology of arterial redistribution is well explained. There is also general agreement about the clinical significance. We observed increased prevalence of abnormal oxytocin challenge test in case of arterial redistribution mainly among growth retarded fetuses and discordant twins. We also found a high probability of fetal hypoxia during labor with an unusually increased incidence of operative delivery for fetal distress when the aortic-cerebral ratio was abnormal. Consideration of Doppler indices is useful for the optimal timing of delivery, especially if invasive tests (amnioscopy, physical or oxytocin challenge test, cordocentesis) are contraindicated.

We concluded that the constant value of aortic-cerebral ratio during the third trimester of gestation reflects the normal fetal arterial blood distribution, while the abnormal aortic-cerebral ratio is associated with an increased incidence of suboptimal perinatal results. We consider the abnormal ratio as a potentially useful marker of impending fetal compromise. Our proposal that increased aortic-cerebral Doppler ratio should be taken into consideration among the indications of labor induction in order to prevent further fetal compromise has been accepted also by international professional medium.

#### IV. PUBLICATIONS

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