# Middle Cerebral Artery, Umbilical Artery Resistance Index Ratio as a predictor of Neonatal Outcome in Patients with Severe Preeclampsia

Thesis
Submitted for partial fulfillment of the master degree
**in Obstetrics and Gynecology**


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**Faculty of Medicine**
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## Protocol of thesis

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# Introduction

Preeclampsia is a pregnancy specific syndrome characterized by reduced organ perfusion secondary to vasospasm and endothelial pathophysiology. Preeclampsia affects 5-10% of pregnancies and is a major cause of maternal and fetal morbidity and mortality **(Sibai B et al., 2005).**

Preeclampsia may cause some complications such as intrauterine growth restriction (IUGR), oligohydramnios, and placental abruption as a result of impaired uteroplacental blood flow **(Harrington K etal., 1995).**

Doppler ultrasound velocimetry of uteroplacental and fetal vessels has become established method of antenatal monitoring allowing noninvasive assessment of fetal circulation. It is indices provide important information about this hemodynamics. Circulatory changes reflected in certain fetal Doppler waveforms, predict adverse perinatal outcome **(Dubiel M et al., 2000)**.

High flow resistance in the capillaries of the terminal villi leads to a low end-diastolic velocity in the umbilical artery and consequent hypoxia **(Weiner et al., 1994).**

Umbilical arteries are the common vessels assessed by Doppler ultrasound. Some studies have showed that Middle Cerebral artery blood flow abnormalities were associated with hypoxia and adverse perinatal outcome **(Kassanos D et al., 2004).**

In experienced hands, Doppler screening of the fetal Middle Cerebral artery wave forms during labour can be useful in the evaluation of intrapartum hypoxia in complicated pregnancies ***(*Kassanos D et al., 2003)**.

Several authors have reported that brain-sparing effect reaches its maximum level 2 or 3 weeks before late decelerations occur on cardiotocogram suggesting that patient with a high risk for unfavorable pregnancy outcome may have MCA blood flow alterations 2 or 3 weeks prior to delivery **(Harrington et al.,1999; Arduiniet &Rizzo., 1992)**.

There are clinical reports showing that compared with MCA indices alone, Middle cerebral artery,umbilical artery RI ratio have better sensitivity for the placental abnormality in high-risk pregnancies **(Ebrashy et al., 2005)**.

Middle cerebral artery,umbilical artery RI ratio reflects not only the circulatory insufficiency of the umbilical velocimetry of the placenta manifested by alterations in the umbilical S/D ratio (ratio of peak systolic blood flow velocity to diastolic velocity) but also the adaptive changes resulting in modifications of the middle cerebral S/D ratio **(Sterne et al. 2001*).***

It was also found that uterine artery Doppler evaluation might have considerable value in the third trimester of high-risk pregnancies and is expected to show the placental perfusion and fetal status while umbilical artery Doppler is expected to show the placental pathology **(Hernandez-Andrade et al., 2002*)***.

# Aim of the Work

The purpose of this study is to detect the relation between the Middle cerebral artery, umbilical artery resistance index ratio in the third trimester of pregnancy complicated with severe preeclampsia and the neonatal outcome.

**Research question:**

In women with sever preeclampsia, does Middle cerebral artery ,Umbilical artery resistance index ratio predicts the neonatal outcome**?**

**Research hypothesis:**

Middle cerebral artery, Umbilical artery resistance index ratio predicts the neonatal outcome in women with sever preeclampsia.

# Patients and Methods

## Type of the study:

A study for accuracy of diagnostic test.

## Study Setting:

Ain Shams Maternity Hospital.

### Study population:

The patients will be recruited from women attending Obstetrics department causality in Ain Shams Maternity Hospital according to inclusion and exclusion criteria which will be enumerated.

### Inclusion Criteria:

1. Pregnant women with viable singleton pregnancy who do not have any obstetric or other comorbidity except for sever preeclampsia.
2. Gestational age between 34 to 40 weeks.
3. Woman with sever preeclampsia diagnosed according to American College of Obstetricians and Gynecologists (ACOG):
    - A previously normotensive woman with two repeated (4-h apart) diastolic blood pressure measurements more than

or equal 110mmHg and systolic blood pressure more than or equal 160mmHg.

- Proteinuria of 3gm/l in 24-hour urine, a urine dipstick showing +3 or +4 in a random urine sample
- Oliguria, with excretion of less than 500 mL of urine in 24 hours.
- Pulmonary edema or cyanosis.
- Impairment of liver function.
- Visual or cerebral disturbances.
- Pain in the epigastric area or right upper quadrant.
- Decreased platelet count.
- Intrauterine growth restriction.
- Not all criteria of sever preeclampsia should be included in the subject but must has the first two criteria.

4. Delivery by cesarean section.

**Exclusion Criteria:**

1. Having any history of hypertension or medical disorders such as hepatic disorders, renal disorder and systemic disease like diabetes mellitus.
2. Receiving medication during the pregnancy apart from iron supplements.
3. Being in active labor or having rupture of membranes.

## Sample Size Justification

Data from a previous relevant study **(Ebrashy et al., 2005)** showed that the prevalence of adverse neonatal outcome (indicated by a cord blood pH < 7.2) among women with severe pre-eclampsia was 66%. The same study showed that the sensitivity of middle cerebral artery / umbilical RI ratio in prediction of such adverse outcome was 64.1%. Calculation according to these values to get the minimal statistically-acceptable figure produced a minimal sample size of 52 case.

## Statistical Methods

Statistical analysis is to be performed using SPSS for Windows version 20.0 and Microsoft Excel version 2010. Difference between two independent groups is to be estimated using unpaired student's t-test (for numeric parametric variables), Mann-Whitney's U-test (for numeric non-parametric variables), and Fischer exact test (for categorical variables). Association and predictability are to be estimated using the ROC curve and stated in terms of sensitivity, specificity, positive and negative predictive values. Significance level is set at 0.05.

## Methodology:

After taking informed written consent, all patients recruited in the study 52 patient with sever preeclampsia will have the inclusion criteria will undergo complete clinical

examination and detailed medical history will be obtained along with necessary lab investigations and ultrasound findings. Each patient will have a case record form in which the following data will be recorded:

- Patient name
- Age
- Parity
- Gestational age

## Clinical Assessment

❖ Laboratory testing:

Included complete blood count, liver function tests, and kidney function tests.

❖ Ultrasound and Doppler studies will be carried out to determine composite ultrasound gestational age amniotic fluid index, estimated fetal weight (EFW).

The ultrasound machine that will be used is Medison Sonoace RS, with a Doppler unit and a 3.5 MHz convex linear probe. The output power of 50mW/cm2 will be used, and the high-pass filter is set to 100Hz.

During the studies, care should be taken to apply minimal pressure to the maternal abdomen with the transducer, as fetal head compression is associated with alterations of intracranial arterial waveforms **(Kirkinen et al., 2006).**

Umbilical artery Doppler resistance index will be estimated by single well-trained sonographer in ultrasound unit at Ain Shams University by application of probe on a free loop of cord. Waveforms will be collected and analyzed in the absence of fetal breathing; on average 3 separate readings. During the examination the women will be in a semi-recumbent position with the head and chest slightly elevated. For measurements of the middle cerebral artery resistance index, an axial view of the fetal head will be obtained at the level of the cerebral peduncles. Color Doppler will be used to visualize the circle of Willis. The angle between the ultrasonography beam and direction of blood flow is always <30 degrees.

Location where the cord is sampled the indices are higher at the fetal than at the placental end of the cord. For Pulsed wave Doppler, a mid-level free floating loop of the cord should be used for sampling when the site of Doppler sampling can be selected. Others recommend using the fetal end of the umbilical cord **(Berkley E et al,.2012)**.

The Doppler sample volume will be placed within 1 cm of the origin of the middle cerebral artery that is identified as a major branch running in direction from the circle of Willis towards the lateral edge of the orbit. For the waveform analysis, maximum and minimum values of the velocity waveforms on the frozen image will be measured by use of electronic calipers of the machine. The C/U RI ratio will be estimated with a cut-

off value of 1.0. Only C/U RIs <1.0 were considered abnormal **(WilliamsWilson S 1995)**.

**Subjects who will contribute in this study will pass through the following steps:-**

- The patient will be delivered by elective cesarean section.
- Spinal anesthesia will be given.
- Incision- to-delivery time doesn't exceed 10 minutes.
- ABG will be taken from the cord(Cord blood sampling: Umbilical cord blood analysis for evaluation of the newborn's acid-base status immediately after delivery is the most objective way of assessing the fetal metabolic condition at birth.**(Armstrong L, Stenson BJ 2007)**.
- Assessment of the neonate by the pediatrician team according to Apgar score at 1, 5 minutes.
- Follow up of the neonate in the first 24 hours.
- Documentation of any need for NICU.

# Outcome:

- ***Primary outcome:*** neonatal outcome will be detected by cord sample pH.
- ***Secondary outcome:*** variables will be early neonatal death, admission to the neonatal intensive care unit and the duration of treatment, Apgar score at 1& 5 minutes, neonatal birth weight.

# Ethical and legal aspects:

## Patient information and informed consent:

Before being admitted to the clinical study, the patient must consent to participate after the nature, scope and possible consequences of the clinical study have been explained in a form understandable to her.

## Confidentiality:

Only the patient initials will be recorded in the CRF, and if the patient's name appears on any other document, it must be kept in a secured place by the investigators.

The investigator will maintain a personal patient identification list (patient initials with the corresponding patient names) to enable records to be identified.

## Protocol approval:

Before the beginning of the study and in accordance with the local regulation followed, the protocol and all the corresponding documents will be declared for Ethical and Research approval by the council of OB/GYN Department, Ain Shams University.

**Study time:**

Recruitment of data will begin once the protocol is approved by the Research and Ethical committee of the department of Obstetrics & Gynecology

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