



ROLE OF FETAL DOPPLER CEREBROPLACENTAL RATIO IN THE SURVEILLANCE OF LATE TERM PREGNANCIES

Thesis

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List of Abbreviations

ACTH	Adrenocorticotrophic Hormone
AFI	Amniotic Fluid Index
ARED	Absent or Reversed End Diastolic Flow
C/U	Cerebral Umbilical Ratio
CPR	Cerebroplacental Ratio
CRH	Corticotrophin Releasing Hormone
CW	Continuous Wave
EFM	Electronic Fetal Monitoring
HPA	Hypothalamic Pituitary Adrenal
ICA	Internal Carotid Artery
MAS	Meconium Aspiration Syndrome
MCA	Middle Cerebral Artery
MSAF	meconium Stained Amniotic Fluid
NICU	Neonatal Intensive Care Unit
PI	Pulsatility Index
RCOG	Royal College of Obstetrics and Gynecology
RI	Resistance Index
S/D	Ratio Systolic /Diastolic Ratio
TNF	Tumor Necrosis Factor
MSL	Meconium stained liquor

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Abstract

Objectives: The present study aimed to assess the value of fetal Doppler cerebroplacental ratio (CPR) measurement in the surveillance of late term pregnancies to determine correlation of CPR with incidence of thick meconium stained liquor.

Subjects And Methods: This was cross sectional study, started with 72 pregnant women, 4 of them dropped out and 68 of those participants were included in this study and admitted to Ain Shams university Maternity Hospital, during the period from December 2018 till May 2019.

Results: results of the study revealed that MCA PI and CPR had significant high diagnostic performance in predicting thick meconium; higher in MCA PI. UA PI had no significant diagnostic performance in predicting thick meconium. MCA PI and CPR had significant moderate diagnostic performance in predicting NICU requirement; higher in MCA PI. UA PI had no significant diagnostic performance in predicting NICU requirement.

Conclusion: MCA PI ≤ 1.06 and CPR ≤ 1.32 had a significant high diagnostic performance in predicting thick meconium; higher in MCA PI. UA PI had no significant diagnostic performance in predicting thick meconium. MCA PI ≤ 1.10 and CPR ≤ 1.39 had a significant moderate diagnostic performance in predicting NICU requirement; higher in MCA PI. UA PI had no significant diagnostic performance in predicting NICU requirement.

Keywords: Fetal Doppler Cerebroplacental Ratio, Meconium Stained Liquor, NICU

INTRODUCTION

The timely onset of labor and delivery is an important determinant of perinatal outcome. Although it has long been known that there is a small absolute increase in perinatal mortality as pregnancies extend beyond the estimated due date (*Vieira & Pasupathy 2016*), the optimum gestational age for beginning close fetal monitoring and the optimum gestational age for intervention rather than continued close fetal monitoring has been more controversial (*Kim et al., 2019*).

The following definitions describe the subgroups of term pregnancy (*ACOG, 2017*):

- Post-term – $\geq 42+0$ weeks of gestation (≥ 294 days from the first day of the last menstrual period and ≥ 14 days from the estimated day of delivery).
- Late term – $41+0$ to $41+6$ weeks of gestation.
- Full term – $39+0$ to $40+6$ weeks of gestation.
- Early term – $37+0$ to $38+6$ weeks of gestation.

One of the most common indications for labor induction is postdate pregnancy; even if there is no consensus about the exact definition of "postdate", the induction is generally performed between 41 and 42 weeks (*Neri et al., 2018*).

-Introduction-

Studies conducted until today identified postdate pregnancy and post maturity as risk factors predisposing to meconium stained liquor (MSL) with subsequent meconium aspiration syndrome (MAS) (**Mittal, 2016**).

Aspiration of meconium typically occurs after fetal hypoxic/ischemic stress leading to intestinal peristalsis, meconium contamination of the amniotic fluid, and gasping respirations that draw the meconium-stained fluid deep into the fetal lung (**Gien & Kinsella 2017**). Meconium contamination of amniotic fluid occurs in 10-15% of all pregnancies, and 5-10% of these infants develop meconium aspiration syndrome and respiratory failure (**Sayad & Silva-Carmona 2020**).

Either non-stress test plus assessment of amniotic fluid volume or the biophysical profile can be used for antenatal monitoring; there is no convincing evidence that one method is superior to the other (**Zafar et al., 2017**).

A few studies had looked into the Doppler blood flow changes in postdate pregnancies. Some demonstrated redistribution of blood flow in the fetal cerebral circulation in postdate pregnancies with adverse prenatal outcome, and such brain sparing phenomenon is thought to result in oligohydramnios. However, others reported insignificant difference in Doppler indices for postdate pregnancies with or without oligohydramnios (**Abd Rabou et al., 2020**).

-Introduction-

Evaluation of the cerebral blood flow in the fetus has become an integrated part of the assessment of high-risk pregnancies. The middle cerebral artery (MCA) has been studied extensively, and its Doppler recordings are incorporated regularly into the management of fetuses at risk of developing placental compromise and fetal anemia (*Aditya et al., 2016*).

It is clear that monitoring the postterm fetus with Doppler ultrasonography of the umbilical artery has no proven benefit (*Alfirevic et al., 2017*).

Combining the Doppler waveform analysis of the middle cerebral artery (MCA) with that of the umbilical artery (UA) by a common cerebroplacental ratio, i.e. the ratio of their pulsatility indices has been suggested as a useful clinical simplification (*Ebbing et al., 2007*).

The cerebroplacental ratio is considered an earlier predictor of adverse outcome than the biophysical profile, umbilical artery, or middle cerebral artery. CPR should be considered as an assessment tool in fetuses undergoing third trimester ultrasound examination, irrespective of the findings of individual umbilical artery and middle cerebral artery measurements (*Ghi et al., 2016*).

PROTOCOL



PROTOCOL OF ATHEIS FOR PARTIAL FULFILMENT OF MASTER DEGREE IN OBESTETRICS & GYNECOLOGY

Title of the Protocol: Role of fetal Doppler cerebroplacental ratio in the surveillance of late term pregnancies.

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What is already known on this subject? AND What does this study add?

Postterm pregnancy is associated with maternal, fetal, and neonatal complications. Many of the complications are sequelae of either excessive fetal growth or placental insufficiency. This study aims at determining the association of fetal doppler cerebro-placental ratio in a homogenous group of uncomplicated pregnancies at 41 to 41+6 weeks of gestation with the incidence of thick meconium stained liquor. The correlation with incidence of passage of thick meconium-stained liquor in labor will be analyzed to decide if this parameter is useful in the surveillance of late pregnancies.

1. INTRODUCTION

The timely onset of labor and delivery is an important determinant of perinatal outcome. Although it has long been known that there is a small absolute increase in perinatal mortality as pregnancies extend beyond the estimated due date, the optimum gestational age for beginning close fetal monitoring and the optimum gestational age for intervention rather than continued close fetal monitoring has been more controversial. (*ACOG, 2013*)

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- Postterm – $\geq 42+0$ weeks of gestation (≥ 294 days from the first day of the last menstrual period and ≥ 14 days from the estimated day of delivery).
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- Early term – 37+0 to 38+6 weeks of gestation.

One of the most common indications for labor induction is postdate pregnancy; even if there is no consensus about the exact definition of "postdate", the induction is generally performed between 41 and 42 weeks. (*Neri and Facchinetti, 2018*)

In the United States, birth certificate data indicate that 0.40 percent of pregnancies deliver at ≥ 42 weeks and 6.5 percent deliver at 41 weeks. A study of birth rates ≥ 42 weeks in 13 European countries observed a wide range across the continent: from 0.4 and 0.6 percent in Austria and Belgium to 7.5 and 8.1 percent in Sweden and Denmark. (*Martin et al., 2017*)

One of the most important factors impacting prevalence of postterm pregnancy is whether early ultrasound assessment of gestational age is performed routinely, as this tends to reduce the prevalence compared with menstrual dating. (*Whitworth et al., 2015*)

The majority of postterm pregnancies have no known etiology. One-third to one-half of the variation in postterm birth in a population can be attributed to maternal or fetal genetic influence on the initiation of parturition. (*Oberg et al., 2013*)

In rare cases, postterm pregnancy has been attributed to defects in fetal production of hormones involved in parturition. (*Liggins et al., 1967*)

The diagnosis of pregnancy $\geq 42+0$ weeks of gestation is based on the clinician's most accurate estimate of the patient's delivery date (EDD). For most pregnancies, the most accurate EDD is based on an ultrasound examination performed before 22+0 weeks of gestation if this EDD differs from that calculated from menstrual dating by more than expected. (*Morken et al., 2011*)



Postterm pregnancy is associated with maternal, fetal, and neonatal complications. Many of the complications are sequelae of either excessive fetal growth or placental insufficiency. (*Rosen and Dickinson, 1992*)

Pregnancies that reach 41+0 weeks of gestation can be induced or managed expectantly with ongoing fetal assessment and intervention if spontaneous labor does not occur by a predefined gestational age or fetal assessment is not reassuring. In the low-risk posttermgravida, both of these approaches are associated with low absolute rates of adverse outcome. (*Middleton et al., 2018*)

Patients should be counseled about what these approaches involve (labor induction with/without cervical ripening agents, type and frequency of antepartum fetal and maternal monitoring) and the maternal and fetal benefits and risks of both approaches.

Expectant management is the alternative to induction. Expectantly managed pregnancies typically undergo twice-weekly fetal assessment beginning at 41+0 weeks (or shortly thereafter), with intervention if spontaneous labor does not occur by a predefined gestational age or fetal assessment testing is abnormal. (*Alfirevic and Walkinshaw, 1995*)

Either non-stress test plus assessment of amniotic fluid volume or the biophysical profile can be used for antenatal monitoring; there is no convincing evidence that one method is superior to the other. (*Alfirevic and Walkinshaw, 1995*)

It is clear that monitoring the postterm fetus with doppler ultrasonography of the umbilical artery has no proven benefit. (*Kauppinen et al., 2016*)

Evaluation of pulsatility indices of the uterine arteries, middle cerebral artery, descending aorta, ductus venosus, and inferior vena cava is also may be not useful. (*Kauppinen et al., 2016*)

This observational study aims at determining the association between fetal cerebroplacental ratio in a homogenous group of uncomplicated pregnancies at 41 to 41+6 weeks with incidence of passage of thick meconium-stained liquor in labor to estimate the value of this ratio in the surveillance of late pregnancy.

2. AIM/ OBJECTIVES

In the surveillance of late term pregnancies, the aim of this study is to assess value of fetal doppler cerebroplacental ratio measurement.

Research hypothesis:

In women with late term pregnancy, the fetal doppler cerebroplacental ratio measurement, may be useful as a surveillance tool.

Research question:

In women with late term pregnancy, may the fetal doppler cerebroplacental ratio measurement be useful as a surveillance tool?



3. METHODOLOGY:

Patients and Methods

Type of Study: Observational cross sectional study.

Tim of study: start at December 2018

Study Setting: The study will be conducted in the labor ward at Ain Shams university maternity hospital.

Study Population: women with late term pregnancy attending Ain Shams university maternity hospital with the following criteria:

Inclusion criteria:

1. Women pregnant at 41 to 41+6 weeks of gestation.
2. Women with singleton pregnancy.
3. Women with correctly estimated gestational age calculated from the first day of regular last menstrual period and confirmed or modified by an early ultrasound examination before 20 weeks gestation.
4. Women with no gross fetal abnormalities found on routine anomaly scan at 20 weeks.
5. Vertex presentation.
6. Average fetal weight.

Exclusion criteria:

1. Women with significant medical complications such as DM, HTN, .. etc.
2. Women with prelabor rupture of membranes.
3. Antepartum hemorrhage.
4. Patients with a uterine scar or any condition preventing induction of labor.
5. Fetal distress.
6. IUGR or macrosomic baby.
7. Women with CTG category III and IV.

Sampling Method: Convenient sample.

Included 68 women with late term singleton pregnancy and gestation age correctly dated at the time of the first trimester nuchal scan between 10 and 14 weeks.

Sample Size: This study will be conducted on 68 late term pregnant women.

Sample Justification: Using Medcalc program, setting alpha error at 5% and power at 80%. Results from previous study (*Lam et al., 2005*), showed that middle cerebral artery pulsatility index (MCA PI) has an area under the curve (AUC = 0.74) in discriminating thick meconium stained liquor from normal cases with estimate 22% prevalence of thick meconium stained liquor of cases. Based on this the needed sample is 68 postdates includes 15 with thick meconium stained liquor.

Ethical Consideration: This study will be done after approval of the ethical committee of the department of obstetrics and gynecology, faculty of medicine, Ain Shams University. Informed consent will be taken from all participants before recruitment in the study, and after



explaining the purpose and procedures of the study. The investigator will obtain the written, signed informed consent of each subject prior to performing any study specific procedures on the subject. The investigator will retain the original signed informed consent form. All laboratory specimens, evaluation forms, reports, video recordings and other records that leave the site will not include unique personal to maintain subject confidentiality. The study will be based on the investigator self-funding.

Study Procedures: late term pregnant women at 41 to 41+6 weeks of gestation will be asked to attend 2 days before induction of labor and will be subjected to detailed history taking, examination and routine investigations.

- **Study Interventions:** Ultrasound and doppler study at the fetomaternal unit, Ain Shams university will be done by a single sonographer using Samsung H60 machine, convex probe: 2-8 MHz
- The following will be assessed:
 1. Amniotic fluid volume (AFV)
 2. Gestational age determination.
 3. Fetal weight estimation.
 4. Middle cerebral artery pulsatility index (MCA- PI).
 5. Umbilical artery pulsatility index (UA- PI)
 6. Cerebroplacental ratio (CPR)
 7. Cardiotocography (CTG).
- Doppler study of the middle cerebral artery.
The fetal head should be in the transverse plane. An axial section section of the brain, including the thalami and the sphenoid bone wings, should be obtained and magnified. The MCA vessels are often found overlying the sphenoid bone near the base of the skull. The reading should be obtained close to its origin from the internal carotid artery. (Rossi, 2015)
- Doppler study of umbilical artery
Ideally the measurements should be made in the free loop of the cord. The umbilical arterial waveform usually has a saw tooth pattern with flow always in the forward direction. (Paudel, et al, 2010)
- Amniotic fluid index:
The uterus is divided into four quadrants with the linea nigra and a mediolateral line through the umbilical acting as the vertical and horizontal axes respectively. The deepest pocket devoid of an umbilical cord and fetal parts is measured in the vertical dimension. Measurement of the four pockets is in centimeters. The sum of the four quadrant measurements is the AFI. (Nabhan and Abdelmoula, 2008)
- Cerebroplacental ratio:
It is calculated by dividing the doppler pulsatility index of the middle cerebral artery (MCA) by the umbilical artery (UA) pulsatility index:
$$CPR = \frac{MCA\ PI}{UA\ PI}$$
 (Berg, et al, 2009).

Induction of labor will be done according to protocol of Ain Shams maternity hospital labor ward at 41 to 41+6 weeks of uncomplicated pregnancy.

Then delivery will be attended to observe any intra-partum fetal distress as determined by intermittent fetal heart auscultation, CTG, or meconium staining of the amniotic fluid. Also, the route of delivery will be registered.