



INDUCTION OF LABOUR: PREDICTING PERINATAL
OUTCOME VIA CEREBROPLACENTAL RATIO
AMONG OBSTETRIC PATIENTS IN HOSPITAL
TENGGU AMPUAN AFZAN

BY

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ABSTRACT

This research sought to evaluate doppler velocimetry studies of the placenta and the fetal circulation that provide important information regarding the fetal well-being. When applied in appropriate conditions it may provide an opportunity to improve the perinatal outcome. The objectives were to assess the usefulness of cerebroplacental ratio (CPR) Doppler in predicting perinatal outcomes among women who were scheduled for induction of labor. There were 203 antenatal women recruited for CPR Doppler studies at 37week and above gestations. CPR less than 1 was taken as predictor of adverse perinatal outcomes. The adverse perinatal outcomes were evaluated by intra-partum cardiotocograph (CTG), mode of delivery, meconium-stained liquor, arterial cord blood pH, Apgar score at 5 minutes and admission to neonatal intensive care unit (NICU). Result showed that, low CPR was significantly associated with abnormal intrapartum CTG ($P < 0.001$), cesarean or operative deliveries for fetal compromised ($P < 0.001$) and low arterial cord blood pH ($P < 0.001$). In conclusion, CPR was a valuable investigation in predicting the perinatal outcomes prior to induction of labor.

APPROVAL PAGE

I certify that I have supervised and read this study and that in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Master of Obstetrics and Gynecology.

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DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other institutions.

Mohd Fairudzi Afzanizam Bin Salleh

Signature

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LIST OF ABBREVIATION

AUROC	Area Under the Receiver Operator characteristic Curve
bpm	Beat per minutes
CTG	Cardiotocography
CPR	Cerebroplacental Ratio
DM	Diabetes Mellitus
HTAA	Hospital Tengku Ampuan Afzan
IUGR	Intra uterine growth restriction
KHz	Kilohertz
MCA	Middle Cerebral Artery
MoM	Multiple of the Median
NICU	Neonatal Intensive Care Unit
PI	Pulsatility Index
PIGF	Placenta Growth Factor
PROM	Premature Rupture of Membrane
SCN	Special Care Neonatal Unit
SD	Standard Deviation
SOGC	Society of Obstetrician and Gynecologist of Canada
UA	Umbilical Artery

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF THE STUDY

The antepartum fetal assessment has become a critical importance in the management of pregnancy (Shaheen, Bano, Ahmad & Singh, 2014). In pregnancy, the fetus obtained adequate metabolic and oxygen from the placenta until birth for growth or fetal well-being. However, the fetal well-being will be affected if the placenta function affected. This is the major risk factor for adverse obstetric and perinatal outcomes and stillbirth (Dunn, Sherrell, & Kumar, 2017). Previously, the clinical assessment, fetal cardiotocography, biophysical profile and ultrasound have been used for assessing fetal well-being. The main purpose of fetal well-being assessment is to evaluate pregnancy, which is at risk of fetal hypoxia, or fetal acidosis that commonly contributes to fetal loss. The assessments help in reducing perinatal morbidity and mortality (Mehta, Vyas, Chauhan, Shah, & Varia, 2013).

Doppler ultrasound of the utero-placental, umbilical and other fetus vessels has become an established method of antenatal monitoring, allowing non-invasive method to assess fetal circulation (Najam, Gupta, & Shalini, 2016). Recently, cerebroplacental ratio (CPR), determined by the color Doppler has proven to be a good predictor of fetal well-being (Shaheen et al., 2014). The CPR has better prediction of adverse perinatal outcomes than its individual component or conventional anthropometric measurements (Dunn et al., 2017). CPR is the ratio of pulsatility index of the middle cerebral artery (MCA-PI) to pulsatility index of the

umbilical artery (UA-PI) (Dunn et al., 2017). It measures the proportion of blood flow supplying the fetus's brain and placenta. Two different mechanisms occur in early phase of fetal hypoxia, which are: reduces flow resistance in the middle cerebral artery (brain sparing effect) and increases flow resistance in the placental. The redistribution of blood flow mechanisms will results in low CPR value (<1) (Shaheen et al., 2014).

The main objective of this study is to determine the association of fetal CPR and perinatal outcomes among obstetrics patients who were scheduled for induction of labor in Hospital Tengku Ampuan Afzan. The women recruited were those admitted for induction of labor for several indications such as hypertension in pregnancy, diabetes in pregnancy, premature rupture of membrane (PROM), oligohydramnios, intrauterine growth restriction (IUGR) fetus, small for gestational age (SGA) fetus, postdate pregnancy and others. We proposed those with a low CPR (<1) is associated with adverse perinatal outcomes. The adverse perinatal outcomes measured include were; pathological CTG, meconium-stained liquor, Apgar scoring (<7 at 5min), arterial cord blood pH value and admission to NICU.

1.2 GENERAL OBJECTIVE

To assess the value of CPR in predicting the perinatal outcome among obstetrics patients who undergo induction of labor in Hospital Tengku Ampuan Afzan

1.3 SPECIFIC OBJECTIVES

- 1- To measure the incidence of abnormal CPR (<1) among various indications of labour induction.
- 2- To measure the incidence of adverse perinatal outcomes among various indications of labour induction in relation to the CPR value (<1) or (≥ 1):
 - Pathological CTG
 - Cases of meconium staining
 - Apgar scoring
 - Arterial blood pH value
 - Admission to NICU

CHAPTER TWO

LITERATURE REVIEW

The Doppler velocimetry in obstetrics is a non-invasive procedure to assess normality of the fetal and uteroplacental circulation indirectly (Paudel, Lohani, Gurung, Ansari, & Kayastha, 2010). In high-risk pregnancies, the use of doppler velocimetry appears to improve obstetrics care outcomes and reduces prenatal death. An obstetrician main concern is early detection of at risk fetus before an insult should happen (Allam & Maarouf Taiseer, 2015).

CPR have been reported to have higher sensitivities and specificities for prediction of fetal prognosis compared to umbilical velocimetry alone. It reflects not only the circulatory insufficiency of the placenta but also reflects the adaptation of circulation resulting in modification of the middle cerebral artery velocimetry (Yalti, Oral, Gurbuz, Ozden, & Atar, 2004). In a prospective study, CPR was proven to be most sensitive (sensitivity 95.6 %). It was more sensitive in predicting any adverse outcome than either UA-PI (sensitivity 91%) or MCA-PI (sensitivity 87.5%) alone (Vishwekar, Sudha, & Jadhav, 2016).

Adverse perinatal outcomes were often associated with an abnormal CPR with overall sensitivity was 62%, specificity was 80%, positive predictive value was 62% and negative predictive values was 80% respectively (Shaheen et al., 2014). There were varieties of abnormal CPR threshold used in studies which were described as < 5th centile, <10TH centile, < 0.90, ≤ 1.0, < 1.05, < 1.09, < 1.1, < 1.3, < 0.6765 MoM.

The variation of these CPR value are due to different characteristic among control group in the studies (Dunn et al., 2017). The characteristics were resulted from three characteristic of Doppler measurement. The first characteristic is when the UA-PI value in higher range while the MCA-PI value is in the lower range of distribution curve resulting in low CPR value. Then second characteristic is when the UA-PI value is normal but the MCA-PI is low and the third characteristic is when there is an abnormally higher UA-PI and an abnormally lower MCA-PI (DeVore, 2015). Many studies used $CPR < 1$ as abnormal, which was also used in our study (Bligh, Greer, & Kumar, 2015)

In a prospective cohort observational study at Al- Zhraa University Hospital, among the high-risk pregnancies showed an association of abnormal CPR with adverse perinatal outcome. The association were statistically significant (p value < 0.005) with pregnancy-induced hypertension (PIH), diabetes in pregnancy (DM), intrauterine growth restriction (IUGR) fetus, caesarean deliveries due to fetal distress, low birth weight deliveries, low 5 minutes APGAR score and neonatal intensive care unit (NICU) admission (Allam & Maarouf Taiseer, 2015).

Abnormal CPR was found to be associated with intrapartum fetal heart rate abnormalities, where the likelihood was more than two fold. The author concluded that low CPR had higher sensitivity (74.1%) and negative predictive value (81%) in the prediction of intrapartum abnormal fetal heart rate patterns as compared to MCA-PI or UA-PI Doppler indices alone (Ropacka-Lesiak, Korbelak, Swider-Musielak, & Breborowicz, 2015). CPR in comparison to its components has higher sensitivity and negative predictive value in prediction of IUGR, operative delivery for fetal distress, low apgar score, meconium aspiration syndrome and NICU admission (Najam et al., 2016).

There was significant association between abnormal CPR and mode of delivery. Delivery rate via caesarean section due to fetal distress were increased in abnormal CPR value patients. CPR shown to be an independent predictor of caesarean section for intrapartum compromise with an area under the receiver operator characteristic curve (AUROC) of 0.69 (Prior, Mullins, Bennett, & Kumar, 2013). At term, low CPR was also independently associated with the need for operative delivery for presumed intrapartum fetal compromise and with NICU admission regardless of the fetal weight. The rates of caesarean section for presumed fetal compromise were significantly higher in appropriate-for-gestational-age fetuses with low CPR MoM (22.3%) compared to small-for-gestational-age fetuses with normal CPR MoM (17.3%) (Khalil et al., 2015).

Prior et al.,(2013), showed that lower pre - labor CPR was significantly associated with Apgar score < 7 at both 1 minute (5.1%, $p < 0.001$) and 5 minutes (27.5%, $p < 0.001$). Neonates born likely to develop acidosis during intrapartum in the low CPR as compared to normal CPR. The differences were significant across the each parameter: UA pH <7.2 (39.1%), base excess <-12 mEq/L (34.8%), pO₂ <15 mmHg (43.5) and pCO₂ > 45 mmHg (44.9%), (All $p < 0.05$) (Ropacka- Lesiak et al., 2015).

Study also reported an association of abnormal CPR with NICU admission. Lower fetal CPR, was independently associated with the need for operative delivery due to fetal compromise as well as neonatal unit admission. The higher umbilical artery PI MoM, lower middle cerebral artery PI MoM and lower cerebroplacental ratio MoM were associated significantly with the babies requiring neonatal unit admission (Khalil et al., 2015).

Study among 50 high risk women in third trimester who were diagnosed with gestational hypertension and pre-eclampsia showed higher caesarean rate significantly ($p < 0.001$), lower apgar score at 1 and 5 minutes and lower pH umbilical cord blood in $CPR < 1$ group. Neonatal intensive care unit admission also was found to be higher in similar group (Yalti et al., 2003). Another study in 90 pregnancies at 30-40 weeks gestation that had been diagnosed clinically as IUGR showed CPR has 100% specificity and positive predictive value in diagnosing small for gestational age and predicting adverse perinatal outcome however has low sensitivity (44.4%) and negative predictive value (64.3%) in diagnosing IUGR (Bano, Chaudhary, Pande, Mehta, & Sharma, 2010).

In 2016, a prospective observational study on the role of fetal arterial Doppler study in decision making of high risk pregnancy has proven that 55.26% patient with abnormal perinatal outcome showed $CPR < 1$ compared to 8.06% in normal CPR cases (Patel, Deliwala, & Pandya, 2016). Thus, the CPR seems to be valuable in predicting perinatal outcomes of high-risk pregnancy. Thus, in this study we evaluate the importance of CPR in predicting the perinatal outcome among high-risk obstetrics patients that undergo induction of labor in Hospital Tengku Ampuan Afzan (HTAA).

CHAPTER THREE

METHODOLOGY

This prospective observational study was conducted in Hospital Tengku Ampuan Afzan from January to September 2017. The sampling was discontinued once the targeted sample size achieved. The patients were followed till delivery and their perinatal outcomes were recorded.

3.1 INCLUSION & EXCLUSION CRITERIA

Pregnant women who undergone induction of labor, age more than 18 years old with singleton pregnancies and gestational age 37 weeks and above were included in the study. We excluded all cases with congenital anomalies, abnormal finding of umbilical artery Doppler (absent end diastolic flow or reverse end diastolic flow), abnormal CTG prior to induction of labor and women planned for elective caesarean section.

3.2 STUDY PROTOCOL

3.2.1 Cerebroplacental Ratio Measurement

All patients recruited in this study were those who attended screening center and admitted for induction of labor. The demographic data and antenatal background of the patient were obtained. Usual ultrasound scan were performed to all cases to assess the fetal wellbeing. The umbilical artery (UA) and fetal middle cerebral arteries

(MCA) were examined with 4.0 KHz curvilinear probe using Voluson P8 color doppler machine. It was done by the same researcher in screening centre, under supervision of the IIUM maternal-fetal medicine consultant. The angle of isonation was kept at <20 degree in all cases. The doppler velocimetry of UA were obtained from free-floating loop of the umbilical cord during fetal quiescence. The MCA was visualized using color flow mapping in an axial section of the brain. The doppler beam was directed along the MCA and the sample volume was placed over the proximal section where the MCA emerges from the circle of Willis at the level of cerebral peduncles. MCA with flow towards the probe was chosen. The average of three measurements were recorded. CPR was calculated either $CPR \geq 1.0$ (no brain sparing effect) and $CPR < 1.0$ (brain sparing effect).

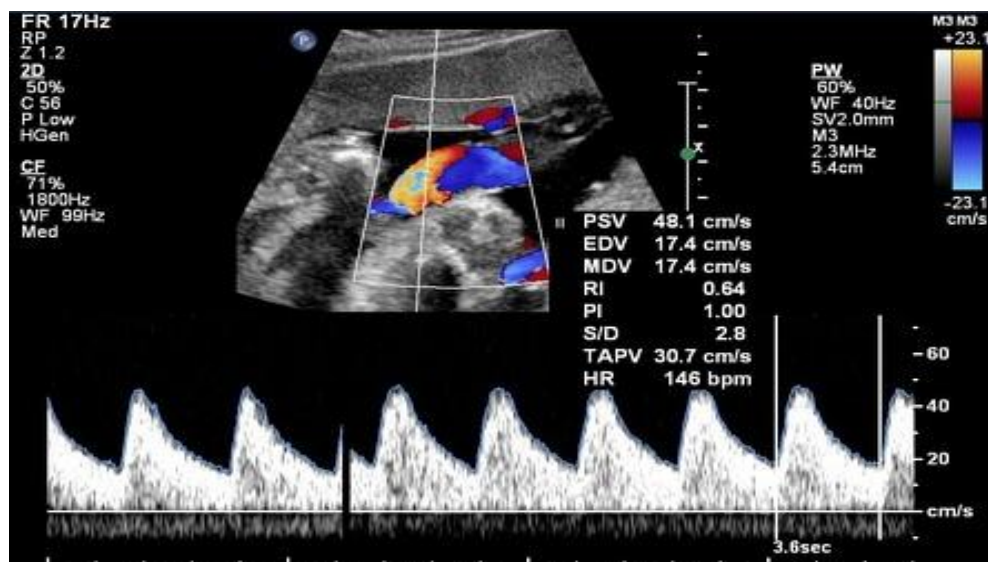


Figure 3.1: Normal umbilical artery Doppler

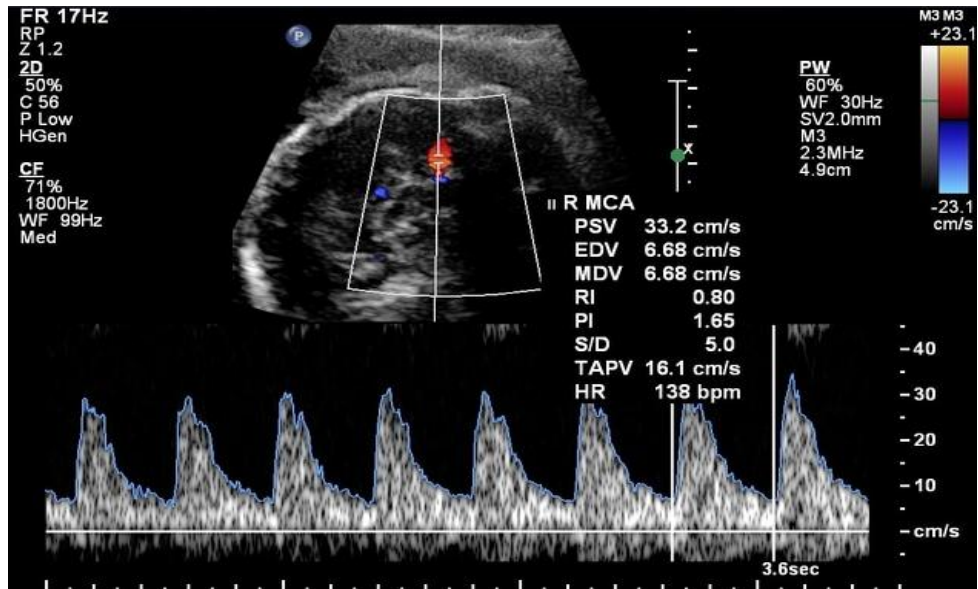


Figure 3.2: Normal Middle Cerebral Artery Doppler

3.2.2 Induction of Labour

Method of induction performed was either by medical (vaginal prostaglandin E2, Prostin) or mechanical induction (foleys catheter) according to department protocol. The fetal cardiotocography (CTG) was done prior and one hour after induction of labour.

3.2.3 Perinatal Outcome

Once patients were admitted in labour room, all intrapartum fetal CTG monitoring, meconium incidence, mode of delivery, neonatal apgar score, arterial cord blood gases and neonatal intensive care unit (NICU) admission were recorded.

3.2.3.1 Intrapartum Cardiotocography

Patient received continuous CTG during intrapartum period. The abnormal tracing recognized and actions taken during intrapartum were recorded. Fetus was considered

compromised if there was present of pathological tracing. CTG is considered pathological if presence of more than one non-reassurance features.

3.2.3.2 Incidence of Meconium

Throughout intrapartum, the significant of meconium staining of the amniotic fluid depends on the grade of meconium and stage of labor. In this study, the incidence of meconium was recorded as either clear liquor or meconium stained liquor.

3.2.3.3 Apgar Score of Neonate

Apgar Score of the neonate at 1 minutes, 5 minutes and 10 minutes were recorded after delivery as shown in table 3.1. Apgar Score of less than 7 at 5 minutes of life was considered as abnormal.

SIGN	0	1	2
COLOR	Blue or pale	Acrocynosis	Completely pink
HEART RATE	Absent	<100	>100
REFLEX IRRITABILITY	No response	Grimace	Cry or active withdrawal
MUSCLE TONE	Limp	Some flexion	Active motion
RESPIRATION	Absent	Weak cry, hypoventilation	Good crying

Table 3.1 Apgar score (American Academic of Paediatric, Committee on Fetus and Newborn, American College of Obstetricians and Gynaecologist and Committee on Obstetric Practice Paediatrics, 2006)

3.2.3.4 Arterial Cord Blood Gases

Arterial cord blood gases were obtained from the umbilical artery right after cutting of the umbilical cord. Arterial blood was aspirated using 1.0 ml heparinized syringes (to prevent blood from clotting). A needle was inserted into the umbilical artery slowly at 45-degree angle to obtain the required amount of blood between 0.2ml to 0.5 ml. The needle was then removed from the syringe and replaced by a cap. The sample was put into an ice-box and sent to the laboratory within 20 minutes. The arterial cord blood gases result was recorded. The pH value of less than 7.2 was considered as abnormal or acidosis.

3.2.3.5 Neonatal Intensive Care Unit admission

Admissions to neonatal intensive care unit (NICU), neonatal ward (SCN) or postnatal wards (PNW) were recorded.

3.3 DATA ANALYSIS

The statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 20 for Windows, software. All the numerical data with normal Gaussian distribution were presented as means (SD) while categorical data were expressed as number (%). χ^2 test was used to determine the significant relationship between two categorical variables. A p value of <0.05 was considered as significant.

CHAPTER FOUR

RESULT

There were total of 203 patients were recruited in the study. They were all adhered to the study.

Table 4.1 Clinical Characteristic of the Study Population

Characteristics	Mean (SD)
Age (years)	28.39 (5.35)
Gestational Age	39.36 (1.55)
Parity	2.48 (1.61)
Body Mass Index(BMI) (kg/M2)	28.48 (5.51)
Haemoglobin	11.61 (1.28)
*Indications of Labour Induction	n (%)
PIH	16 (7.88)
GDM	57 (28.07)
PROM	39 (19.21)
Oligohydramnios	21 (10.34)
IUGR	8 (3.94)
SGA	3 (1.48)
Postdate (EDD+6 days)	50 (24.63)
Others	27 (13.30)

* Some patients had more than one indication for induction of labor

The majority of the patients were overweight and low parity. However there was one patient who was para 12 in the study.

Table 4.2 CPR value in relation to the indications of induction

Risk factors	CPR ≥ 1 n = 210 (%)	CPR <1 n =11 (%)	<i>p-value</i>
PIH	16 (7.6)	0 (0)	0.431
GDM	55 (2.6)	2 (18.2)	0.432
PROM	35 (16.6)	4 (36.4)	0.102
Oligohydramnios	21 (10)	0 (0)	0.327
IUGR	8 (3.8)	0 (0)	0.663
SGA	3 (1.4)	0 (0)	0.859
Postdate (EDD+6 days)	47 (22.4)	3 (27.3)	0.465
Others	25 (11.9)	2 (18.2)	0.394

The patients were induced either by prostaglandin (PGE2) or Foley's catheter. Majority were induced has for diabetes in pregnancy (28.07 %) followed by postdate pregnancy (24.63 %) and premature rupture of membrane (19.21%). There were 18 patients identified whom had more than one indication (8.87%). Twenty-seven (13.3%) patients out of 203 were induced for other indications such as reduced fetal movement at term or prolonged latent latent phase of labor. All patients with hypertension in pregnancy, oligohydramnios, IUGR and SGA had normal CPR (≥ 1). Eleven (5.4%) patients out of 203 had CPR (<1) where most were of PROM and post-date.