INTRODUCTION

Fetuses exposed to placental insufficiency experience progressive oxygen and nutritional deficits, which ultimately lead to hypoxia, hypercapnea and acidosis. It can lead to fetal growth restriction, which affects approximately 8% of all pregnancies and is associated with increased perinatal mortality and morbidity *(Regnault et al., 2002)*.

Intrauterine growth restriction (**IUGR**) is defined by the American College of Obstetricians and Gynecologists as estimated fetal weight (**EFW**) less than that expected for gestational age *(ACOG, 2000)*. In severely premature IUGR fetuses, gestational age at delivery and birthweight have long been recognized as important predictors for survival. In IUGR fetuses between 25 and 29 weeks of gestation, each week of continued gestation decreases perinatal mortality by 48% *(Mari et al., 2007)*. Growth restricted neonates have increased rates of meconium aspiration, hematological and metabolic disorders, cognitive dysfunction and cerebral palsy. Most growth restricted fetuses weigh <2500gm at delivery and the long term effects of low birth weight include increased risks for

coronary diseases, hypertension and diabetes mellitus in adult life *(Barker et al., 1993)*.

Animal studies have shown that fetal hypoxia stimulates chemoreceptors that trigger hemodynamic modifications aimed at protecting areas essential to fetal survival, i.e., brain, heart and adrenals *(Kjellmer et al., 1974)*. This selective vasodilatation, combined with compensatory vasoconstriction of other areas, including kidneys, lungs and intestines, is known as fetal brain sparing or centralization and has been shown in human fetuses also *(Wladimiroff et al., 1987)*.

Currently, Doppler ultrasound is accepted by most as the method of choice for diagnosis and management of pregnancy complicated by placentanl insufficiency *(Pardi et al., 2002)*. Fetal arterial Doppler studies are useful in identifying the typical phases of vascular redistribution seen in fetal centralization. As uterine and placental functions deteriorate, abnormal blood flow is detected in the umbilical artery (UA) and the middle cerebral artery (MCA) *(Harrington et al., 1995)*.

Unfortunately, except for delivery, there are no therapeutic interventions currently available to detain

or reverse the course of placental insufficiency. It is, at present, difficult to accurately determine the transition between fetal adaption to hypoxia and decompensations. Therefore, it is difficult to determine the best management plan for these cases and to decide when to intervene, weighing the risks of prematurity against those of fetal demise or irreversible organ damage *(Pardi et al., 2002)*.

In clinical practice, this adaptive mechanism is generally assessed with Doppler ultrasound as a reduction in the pulsatility index (PI) in the middle cerebral artery *(Ganong, 2003; Pollack et al., 1992; Marsal, 2002)*. In addition, further researches has also suggested that the same process can be documented in different fetal brain arteries *(Dubiel et al., 2002; Figueroa et al., 2007)*.

In the final stages of centralization, end-diastolic ventricular pressure increases, blood ejection during atrial contraction decreases and abnormalities in fetal venous flow become noticeable on venous Doppler studies *(Cheema et al., 2004)*. Doppler studies lead to the clinical recognition of haemodynamic decompensation. With the reduction in the cardiac output, central venous pressure rises, causing an

increase in inferior vena cava reverse flow and absent or reversed flow in the ductus venosus (DV) during atrial systole. This progressive deterioration of blood flow in the precordial veins presumably reflects the aggravation of myocardial dysfunction and is believed to be related directly to the severity of acidemia *(Cheema et al., 2004; Dubiel et al., 2001; Laurichesse et al., 1999)*.

Fetal cerebral venous circulation has previously been explored in fetuses with vein of Galen (VG) aneurism *(Vijayaraghavan et al., 2006)*. The cerebral transverse sinus (CTS) shows a triphasic pulsatile forward flow velocity pattern similar to that described in other fetal venous vessels, the first studies evaluating its blood flow to assess fetal well-being were published at the end this decade *(Laurichesse et al., 1999; Senat et al., 2000)*.

A few studies published in the last 2 years indicate that venous-arterial Doppler ratios may be useful in fetal evaluation. A comparison between Doppler velocimetry of the UA, DV and inferior vena cava in normal pregnancies was done and noting that the UA/DV PI ratio was constant throughout gestation and that the PI of the UA over DV S/A or (S-A)/S

declined with increasing gestational age. This emphasized the importance of testing these ratios in pregnancies with placental insufficiency *(Baschat, 2003)*.

AIM OF THE WORK

The aim of this study was to evaluate, in pregnancies with placental insufficiency, the prediction of acidemia at birth using various Doppler parameters of the ductus venosus, umbilical artery and middle cerebral artery. Specifically, the DV PI/UA PI and DV PI/MCA PI ratios were evaluated and their best cut-off values were calculated.

DOPPLER ULTRASOUND

In 1842, an Australian professor of mathematics and geometry *Dr. Christian John Doppler* first described in detail the effect that now bears the name. **Satomura** was the first describing clinical application of Doppler ultrasound technology in 1959 *(Rosenberg, 1997).*

Doppler velocimetry was first applied to the fetal arteries in 1977 by **McCallum,** who used for the first time the continuous wave Doppler Effect in order to obtain flow velocity in the umbilical artery after delivery. In the same year, **Fitzgerald and Drumm** used pulsatile Doppler to assess blood flow velocity in the umbilical vessels intra-utero, showing for the first time the spectral characteristics of these vessels and describing the usefulness of the new mettod in cases of pre-eclmpsia and intrauterine growth restriction *(Gadelha-Costa et al., 2007)*.

Doppler US offers a unique noninvasive technology for investigating the circulatory system. Doppler ultrasound velocimetry has been extensively used to investigate fetal, feto-placental and uteroplacental circulation. There is ample evidence

associating abnormal Doppler findings with complication of pregnancy and an adverse perinatal outcome *(Nicolaides et al., 2002)*.

Doppler shift is a physical principle that states that when a source of sound waves is moving relative to an observer, the observer detects a shift in the wave frequency. Thus, when a sound wave strikes a moving target, the frequency of the sound waves reflected back is shifted proportionate to the velocity and the direction of the moving target. Because the magnitude and direction of the frequency shift depend on the relative motion of the moving target, their velocity and direction can be determined *(Maulik et al., 1990)*.

In medical application, the Doppler Effect is usually used by insonating the moving blood and assessment of the Doppler shift of ultrasound scattered on erythrocytes. Each single erythrocyte reflects (retransmit) ultrasound in various directions, but the back scattered energy is sufficient for velocity assessment *(Kurjack and Kuspesik, 2004)*.

Instrumentation for Doppler measurement:

A number of techniques have been developed which use the shift in frequency of ultrasound when it is reflected from moving blood. This frequency shift is

known as the (Doppler Effect). Four types of diagnostic Doppler instrument are usually distinguished.

1. Continuous wave Doppler (CW).

2. Pulsed wave Doppler (PW).

3. Duplex Doppler.

4. Color Doppler imaging.

The characteristics of an ultrasound beam, the propagation of ultrasound in tissue and design of the transducer as found in B-mode imaging are all relevant for Doppler techniques (*McDicken et al., 2002)*.

The continuous wave Doppler:

The simplest Doppler device is the continuous wave (CW) flowmeter. One important feature of this device, that it requires two transducers. The master oscillator produces a steady, continuous, sinusoidal waveform that is amplified and used to drive the transmitting transducer at its resonating frequency. The consequent ultrasonic beam hits the moving targets (erythrocyte) that produce reflected and back-scattered echoes. It also hits stationary targets, which can produce much stronger echoes, although they will not have any Doppler shift. It must identify the echoes from moving targets and reject the stationary target

echoes that will be unshifted. In addition it needs to measure the size of Doppler shift (*Evans, 2004)*.

The advantage of continuous wave equipment is relatively inexpensive and portable. The main advantage is that the vessel being studied cannot be simultaneously visualized (*Meire, 1986)*.

Pulsed wave Doppler (PW):

In pulsed Doppler system the same transducer is used to transmit and then to listen for the returning signal. By only allowing the equipment to receive echoes for a short period, the depth from which the echoes arise can be precisely determined *(Maulik et al., 1990)*.

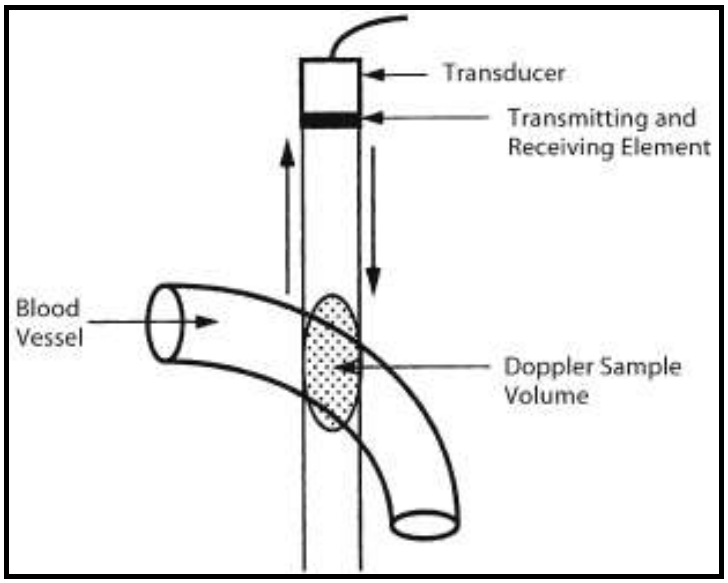

Fig. (1): Pulsed-wave Doppler transducer *(Maulik, 2005)*.

Pulsed Doppler systems have the ability to select the depth from which Doppler information is received, thus allowing analysis of blood flow within a single vessel. To do this the vessel to be studied is first located with continuous wave ultrasound. Next agate is placed over the vessel which passes only signals that are returned within a defined time. The width of the gate (also called the volume box) is adjusted to the diameter of the vessel. The returning Doppler frequency shift echoes are convened electronically and displayed as Doppler shift versus time wave form (*Kremakau, 1990)*.

The rate at which pulses of ultrasound are emitted is known as the pulse repetition frequency (PRF). The higher the PRF the more pulses will be available per cycle, thus giving a better quality signal. This restriction on the PRF is dependant on the depth of the sample volume, the maximum PRF being given by the formula:

$$PRF\ (HZ)=(c.\times d.)/2$$

Where (c.) is the velocity of sound in tissue (1540m/s) and (d.) is the depth (cm) of the structure being investigated.

The minimum PRF allowable must be twice the frequency of Doppler signal. If the PRF is lower, aliasing is produced and failure to obtain the Doppler signal occurs *(Mcparland and Pearce, 1990)*.

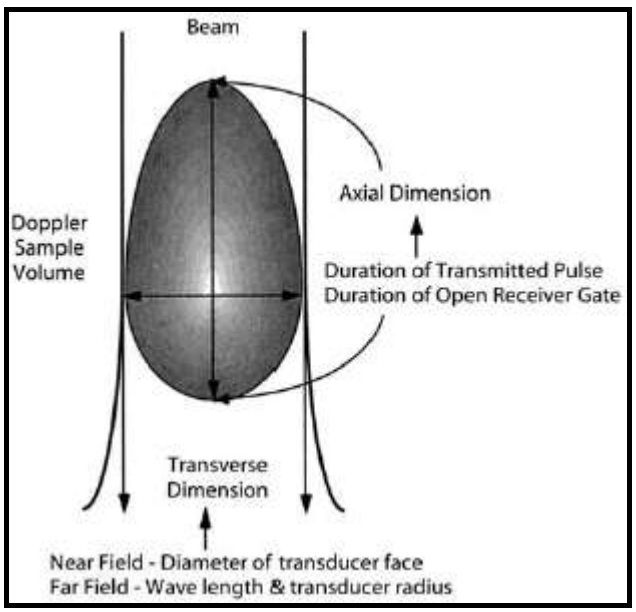

Fig. (2): Doppler sample volume and the factors controlling its dimensions *(Maulik, 2005)*.

Aliasing

Aliasing is the most common artifact encountered in Doppler ultrasound. There is an upper limit to Doppler shift that can be detected by pulsed instruments if the Doppler shift frequency exceeds one half the pulse repetition frequency, aliasing occurs and improper Doppler shift information (wrong direction and wrong values) results. Aliasing can be

eliminated by increasing pulse repetition frequency, increasing Doppler angle (which decreases the Doppler shift for a given flow), or by baseline shifting (*Kremkau, 1990)*.

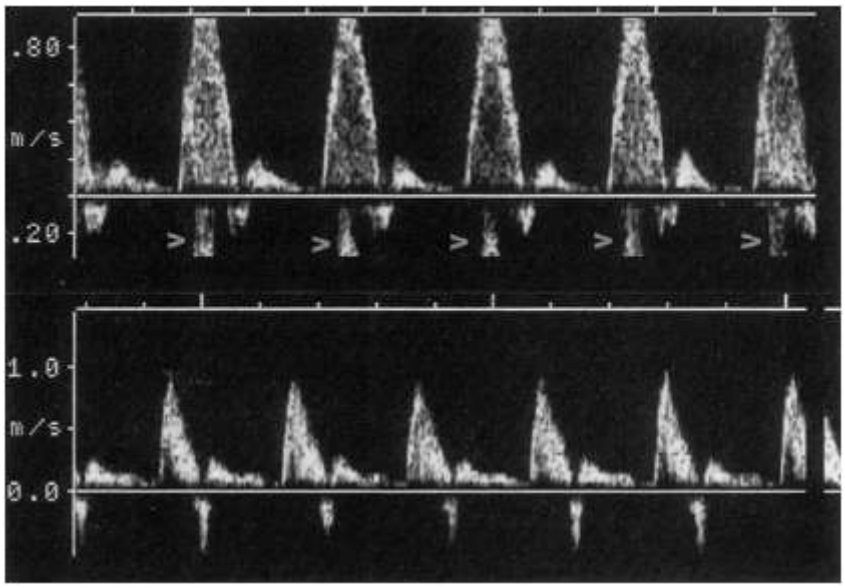

Fig. (3): Example of aliasing and its correction *(Maulik, 2005)*.

Duplex Doppler:

The combination of pulsed Doppler and real time ultrasound is known as a duplex system, and allows simultaneous imaging at low pulse repetition frequently, usually less than 2.5KHz (*Maulik et al., 1990)*.

It allows the precise localization of deep vessel and the positioning of the Doppler volume within it *(Eik-Nes et al., 1980)*.

Color flow Doppler:

It is an attempt to overcome some of the limitation of pulsed Doppler. It was introduced in 1980s and is now a common feature on ultrasound scanners. The key feature is that the search for Doppler shifts is not restricted to a single volume, as in pulsed Doppler, but rather applies to a large region, possibly even the whole image. Each ultrasound line is divided into blocks (typically 50-100 blocks per line) and the echo signals returning from each block are examined for evidence of Doppler shift. If a shift is detected, then a color (typically blue or red) is superimposed on the underlying image. It has become conventional to use red to designate flow towards the probe and blue for flow away from it. The great advantage of color flow mapping is that the signal relies only upon the presence of a Doppler, so that small vessels (e.g., those in the fetal circle of Willis) *(Evans, 2004)*.

Hemodynamic information from Doppler

Doppler US can generate a wide range of haemodynamic information from simple recognition of the presence of flow to the velocity profile and quantification of flow, and assessment of downstream vascular impedence *(Maulik et al., 1990)*.

Velocity calculation:

If the angle between the Doppler beam and the blood vessel is known the frequency can be converted into actual blood velocity using the equation

$$Fd=2\ f\ 0\ v\ \cos\Theta/c$$

Where Fd is the Doppler shift in the frequency, f0 is the frequency of the emitted ultrasound; v is the velocity of the moving target; Θ is the angle between the ultrasound beam and the direction of movement of the target; and c is the speed of sound in tissue.

Velocity measurements have not achieved popularity in obstetric use because of the difficulty of obtaining accurate measurement of the angle insonation *(Evans, 2004)*.

Flow quantification:

Instantaneous flow can be measured by the following equation: $Q_1=A_1.V_1$ where Q_1 is the instantaneous flow, A□(the vascular cross-sectional area at the instant velocity measurement, and V_1 the mean velocity across the vascular cross-sectional area at the instant of the measurement. Unfortunately, there are several technical difficulties with measure-ment of the vessel diameters. The vessels are dynamic