Introduction

Post-term pregnancy is a pregnancy extending beyond 42 weeks or 294 days, from the 1st day of last menstrual period. The incidence of post-term pregnancy is about 10%, although this incidence may represent a three fold or more overestimation because of inaccurate pregnancy dating in older studies. Some studies indicated that the incidence of post-term pregnancy for subpopulations with a reliable menstrual histories and early confirmatory ultrasound dating decreased to about 2% *(Trager et al., 2002)*.

Several studies have concluded that prolongation of pregnancy beyond term is accompanied by a significant rise in perinatal morbidity and morality *(Cunningham et al., 1997)*. Complications such as oligohydramnios, meconium aspiration and fetal asphyxia are more common in post-term pregnancy *(Trager et al., 2002)*. Approximately 10% of fetuses in post-term pregnancy develop dysmaturity, a condition of growth retardation engendered by uteroplacental insufficiency that if undetected could progress to asphyxial damage and possible still birth *(James, 2000)*. It is speculated that the development of oligohydramnios in post-term pregnancies is caused

by compensatory redistribution of fetal blood flow resulting in renal hypoperfusion concomitant with maintaing adequate blood flow to the fetal brain *(Barhava et al., 1995)*.

Pulsed wave Doppler sonographic studies provide a non-invasive method for the assessment of blood flow in the fetal circulation and may provide some insights into the development of oligo-hydramnios in post-term pregnancies *(Selam et al., 2000)*. Meconium staining of amniotic fluid is found in 7-22% of term pregnancies *(Benirnchke, 2001)*.

Meconium can be a marker of fetal compromise or an environmental hazard for the fetus. The incidence of non reassuring cardiotocography in women presenting with meconium stained liquor was significantly higher (9.8% vs 6.4%) *(Wong et al., 2002)*, the relative risk of non-reassuring cardio-tocography in these women increased with more advanced gestation. Association between moderate or thick meconium stained liquor (MSL) and adverse pregnancy outcomes that include low Apgar scores at birth, fetal acidemia and hypoxaemia, emergency caesarean delivery or instrumental delivery for fetal distress, meconium aspiration syndrome and

neurodevelopment handicap have been reported *(Maymon et al., 1998)*.

Management of uncomplicated prolonged pregnancies has always been a dilemma as the current fetal surveillence tests can not accurately identify which pregnancies are at risk for an adverse outcome.

Meta-analysis recommended that further trials are necessary to asses the effectiveness of the antenatal fetal testing methods, as there is no single ideal test yet been devised in evaluating well being of the post-term fetuses *(Palacio et al., 2004)*.

It has been shown that there is a strong correlation between middle cerebral artery blood flow and hypoxia and therefore, standard assessment of at risk fetuses includes evaluation of this vessel. However, information in prolonged pregnancies is scarce *(Arbeille et al., 1995)*.

Middle cerebral artery resistance is known to decrease at the end of pregnancy. This may represent a physiological change associated with an increase in cerebral metabolic requirements, a brain-sparing effect to protect intracranial structures during labour or it may be secondary to the mild placental

insufficiency that occurs at this stage of gestation *(Placio et al., 2004)*.

A new Doppler index, the cerebroplacental ratio, defined as the cerebral resistance index divided by the umbilical resistance index may be the most sensitive Doppler index for predicting fetal compromise than either vessel considered alone, even when umbilical resistance index is within normal range. In spite of its promise, there are relatively few clinical publications related to this index, and in the majority of instances, a comparatively small number of affected cases were enrolled *(Ray et al., 1999)*.

In this study, a trial to provide a fetal surveillance program with specific parameters to identify compromised fetuses so as to individualize management in postdated pregnancies.

Aim of the Work

To evaluate the role of fetal Doppler blood flow resistances indices of middle cerebral, umbilical, renal, aortic arteries cerebroplacental ratio and Amniotic Fluid Index (AFI) in prediction of intrauterine fetal hypoxia and perinatal outcome in medically uncomplicated pregnancies at 41 weeks.

Fetal Growth and Physiology

Cardiovascular System:

The fetal heart forms from a pair of mesor-dermally derived tubes which fuse by approximately 21 days: Thereafter growing differentially, lopping and becoming divided by septa. The ductus venosus allows the flow of well oxygenated blood from the umbilical vein to by pass the liver and reach the right atrium. In the atria, the septum secundum allows the right to left flow of oxygenated blood from the inferior vena cava and is a mechanical obstacle to left to right shunting. The ductus arteriosus shunts approximately 55% of the output of the right ventricle direct to the aortic arch., by passing the lungs, which only receive a small nutritive blood supply. This arrangement allows the developing brain and myocardium to receive the best oxygenated blood, an ingenious adaptation *(Broughton, 1999)*.

Fetal oxygen consumption increases in parallel with body weight to term, and the fetal cardiac output keeps pace with this. As fetal blood O_2 content is 20% lower than in adult, in spite of the higher O_2 affinity of

fetal blood and the higher hemoglobin concentration, fetal cardiac output has to be proportionally higher than adult (Approximately 500ml/kg per minute).

There is increasing myocardial contractility from fetal to adult life, and starling's law appears to hold in the fetal heart from early gestations. Human fetal heart rate decrease progressively from about 14 weeks gestation to approximately 120-160 beats/minute at term, as parasympathetic (vagal) tone increases.

The acute regulation of fetal cardiac output is heavily dependent on heart rate rather than stroke volume *(Broughton, 1999)*.

Fetal oxygen and carbon dioxide handling and control of acid-base balance:

The fetus has a very low PaO_2 (approximately 35mmHg in the umbilical vein) and high $PaCo_2$ (approximately 42mmHg in the umbilical vein). Further hypoxia is thus potentially very dangerous *(Broughton, 1999)*.

Acute severe fetal hypoxaemia is associated with maintained blood flow to the brain, adrenal gland and heart at the expense of other tissues *(Thorburn and Harding, 1994)*. Peripheral chemoreceptors are

activated, there is increased sympathetic tone and in later gestation circulating concentrations of cortisol, catecholamines, angiotensin II and vasopressin rise increasing peripheral resistance *(Teitel, 1996)*. When the hypoxaemia is sever, the deprived tissues may not be able to maintain oxidative phosphorylation, and well shift to anaerobic pathways. Since the fetus has a lesser ability to cope with acid-base disturbances lactic acidaemia can rapidly develop. This shifts the oxy haemoglobin dissociation curve to the right, which will still further lower blood O_2 content. This vicious circle can quickly result in fetal death *(Teitel, 1996)*.

Less severe but chronic hypexaemia is associated with increased erythropoietin concentrations, a slowing of fetal growth and with reduced glycogen stores because of their utilization. Such children have a higher than usual incidence of neurological deficits *(Jacobson, 1991)*.

Fetal acid-base physiology:

The fetus produces carbonic and organic acids carbonic acid (H_2 Co_3) is formed by oxidative metabolism of Co_2. The fetus can rapidly clear Co_2 through the placental circulation, and when H_2 Co_3

accumulates in fetal blood without an increased in organic acids, the result is respiratory acidemia. Organic acids primarily are formed by anaerobic metabolism and include lactic and β-hydroxy butyric acids. These organic acids are cleared slowly from fetal blood and when they accumulate without an increase in H2 Co_3, the result is metabolic acidemia, with the development of metabolic acidemia, bi carbonate (HCo_3) decrease because it is used to buffer the organic acid. An increase in organic acid accompanied by an increase in H_2Co_3 is known as a mixed respiratory-metabolic acidemia.

In the fetus, respiratory and metabolic acidemia, and ultimately tissue acidosis, are most likely part of a progressively worsening continuum. This is different from the adult pathphysiology, in which distinct conditions result in either respiratory (pulmonary disease) or metabolic (diabetes) acidemia. In the fetus, the placenta serves as both the lungs and, to a certain degree, the kidneys. One principal cause of developing acidemia in the fetus is a decrease in utero placental perfusion *(Cunningham et al., 2005)*.

Metabolic acidosis results in decrease in the buffer base, as its various components (bicarbonate,

phosphate, hemoglobin and proteins) absorb the excess of hydrogen ions being released from lactic acid. The normal fetal base deficit is in the region of 7mEq/liter, but when fetal metabolic acidosis occurs, it may exceed 10 or 15mEq/liter. In metabolic acidosis, the PCo_2 may be mildly elevated and of course, the fetal PH will be decreased. Normal arterial blood PH is in the region of 7-28-7-30) *(Shaaban, 2006)*.

Fetal Kidney:

The kidney only receive some 2% of the cardiac output in utero *(Broughton, 1999)*. Glomerular filteration rate (GFR) is very low whether expressed in absolute or relative terms, because of morphological immaturity of the nephrons, low renal perfusion pressure and colloid osmotic pressure and high intrarenal vascular resistance *(Thorburn and Harding, 1994)*.

Human fetal urine production begins around 8 weeks gestation, with excretion into the amniotic sac. Other sources of amniotic fluid are the lungs and respiratory tract, fetal membranes and fetal placental surface.

The neoborn human excrete a highly hypotonic urine with a high free water clearance. The medullary concentration gradient is not established, and the collecting duct is relatively impermeable to orginin vaso pressin (AVP). This may be due to decreased receptor number, and/or the stimulus to response link for AVP may be blunted. From the moment of birth the neonatal kidney must conserve sodium, an unnecessary action in utero. The fractional excretion of sodium is high and is 5-6% in prematurely delivered humans *(Lumbers, 1995)*.

The ability of fetal adrenals to synthesize aldosterone (ALD) in the face of sodium loss rises during gestation and plasma ALD is high at birth. However, this is not translated into sodium retention, possibly because of function immaturity of the distal tubular receptors. Fetal urine mostly contains no glucose as circulating fetal glucose concentrations are relatively low, and, near term, the sodium-dependant glucose transport system appears relatively mature.

The kidney of the fetal lamb can reabsorb 80-100% of the filtered bicarbonate load, however, the low fetal renal clearance of phosphate means that the

response to metabolic acidosis is limited *(Lumbers, 1995)*.

The renal renin-angiotensin system is functional from 5 weeks gestation in human. Vasosilator prostaglandins can also be synthesized intra renally from the first third of gestation *(Broughton, 1999)*.

Fetal central nervous system:

Brain development proceeds by a cascade of neuronal induction, neuroblast proliferation, neuronal migration and selective aggregation, followed by differentiation and the formation of specific patterns of connection, neuronal death and selective synapse elimination, and myelination in the fetal central nervous system (there is thought to be no myelination until approximately 8 weeks gestation *(Jacobson, 1991)*.

The planter and palmer reflex can be elicited at 8 weeks. Fetal movements are detected by ultrasound from approximately 8 weeks gestation. These begin as simple "startle' movements, and by 16 weeks have become complex and co-ordinated including sucking and swallowing *(Jacobson, 1991)*. The fetal brain grows rapidly during the second and third trimesters, and

neuronal numbers are established by 8 months. There are three main brain growth spurts before birth:

12-18 weeks, (neuroblast proliferation), approximately 25 weeks, (glial proliferation), and finally from 30 weeks, the cerebellar growth spurt. The brain is protected against inadequate utero placental blood flow and oxygen delivery as far as possible so babies with severe intrauterine growth retardation have high head circumference to birth weight ratios. The functional maturation of the brain, and glial cell proliferation are not complete until well after birth *(Broughton, 1999)*.

The Newborn Infant

Changes in the immediate postnatal period initiation of air breathing:

The hypoxaemia and acidaemia associated with vaginal delivery sensitize the medullary chemo-receptor. Body temperature begins to fall immediately after delivery. These factors appear to be the most important in stimulating the first breath *(Teitel, 1996)*.

This requires a major effort and the generation of a negative intra thoracic pressure of -40 to -60 cm of water since lung compliance is very low. Surfactant is released during the first lung expansion, lowering surface tension, which makes subsequent breath easier and maintain lung stability *(Teitel, 1996)*.

Aeration of the newborn lung is not the inflation of a collapsed structure, but instead, the rapid replacement of bronchial and alveolar fluid by air, after delivery, the residual alveolar fluid is cleared through the pulmonary circulation and, to a lesser degree through the pulmonary lymphatics *(Chernic, 1978)*. Delay in removal of fluid from the alveoli

probably contributes to the syndrome of transient tachy pnea of the neoborn. As fluid is replaced by air, the compression of the pulmonary vascular is reduced considerably and in turn, resistance to blood flow is lowered. With the fall in pulmonary arterial blood pressure, the ductus arteriosus normally closes *(Cuningham et al., 2005)*.

Methods used to evaluate newborn condition:

APGAR score:

A useful clinical tool to identify those neonates who require resuscitation as well as to assess the effectiveness of any resuscitative measures is the Apgar scoring system *(Apgar, 1953)*. Table (1) showing each of the five identifiable characteristics, heart rate, respiratory effort, muscle tone, reflex irritability, and color is assessed and assigned a value of 0 to 2. The total score, based on the sum of the five components is determined 1 and 5 minutes after delivery.