

INTRODUCTION

Parturition is a multifactorial, physiological process involving numerous interrelated maternal and fetal pathways. It has been proposed that there are several stages that promote the myometrium to a contractile state, including the upregulation of receptors, prostaglandin production, and increased formation of intracellular contraction-associated proteins. The exact trigger for uterine contractions and which pathway is pre-eminent is not yet clear. Cervical ripening is independent of the initiation of uterine contractions, although the pathways are not yet fully known, it does involve the release of proinflammatory cytokines, leukocyte infiltration into the cervix, the release and activation of extracellular matrix metalloproteinases, and other proteins and glycoproteins (*Gelisen, 2005*).

Drugs that act upon the pregnant uterus can be thought of as modifiers of these endogenous physiological pathways controlling normal myometrial contractility and cervical ripening. These drugs may be functionally classified into agents used for the induction and augmentation of labor, for the termination of pregnancy, to treat postpartum haemorrhage, and to treat threatened preterm labor (*Gelisen, 2005*).

Post-term pregnancy is defined as gestation lasting beyond 42 full weeks (>294 days). Diagnosis of every pathological risk that might delay labor is not yet possible, but delay in this physiological event can cause serious fetal and maternal

problems. Large surveys have shown that 1.86 and 2.26 per 1000 deliveries are stillbirths at 41 and 42 completed weeks of gestation, respectively (**Ingemarsson and Kallen, 1997**).

Compared with deliveries at 40 weeks of gestation, the risk of macrosomia, operative delivery, admission to neonatal intensive care units, and neonatal sepsis increases with every further gestational week (**Alexander et al., 2000**).

The use of misoprostol for labor induction with a living fetus was first described in 1992, in the pioneering study by **Margulies et al. (1992)**. Since then, decreasing doses have been proposed and labor induction with misoprostol has been favourably compared with other methods (**ACOG committee opinion, 2000 & 1999**).

Induction of labor using medication involves the stimulation of uterine contractions to produce delivery before the onset of spontaneous labor. Two most common prostaglandins analogues (PGs) currently utilized as cervical ripening and labor inducing agents are misoprostol (PGE1) and dinoprostone (PGE2). Misoprostol is an effective agent for cervical ripening and labor induction in mother with viable pregnancies (**Blanchard et al., 2002**).

A comprehensive review of randomized controlled trials in 1994, concluded that labor should be routinely induced once pregnancy has continued beyond 41 full weeks of gestation (**Crowley, 2001**).

After induction at 41 weeks there was a lower incidence of neonatal morbidity without any significant change in vaginal delivery rates or duration of hospital stay (**Parry et al., 1998 – Seyb et al., 1999 – Maslow and Sweeny, 2000**).

They mentioned five primary outcome of ineffectiveness and complication of use of misoprostol such as uterine hyperstimulation with fetal heart rate changes, increased incidence of cesarean section, serious neonatal morbidity (seizures, birth asphyxia) or perinatal death, serious maternal morbidity or death and vaginal delivery not achieved within 24 hours (**Blanchard et al., 2002**).

Rayburn, in 1993, said that to reduce the incidence of contractility disturbances and neonatal complications, 25 mcg is the recommended dose of vaginal misoprostol for induction of labor (**Rayburn, 1993**).

Many studies have suggested the possibility of sublingual administration of misoprostol for labor induction (**Hofmeyr and Gulmezoglu, 2002; Kelly et al., 2001 and Fletcher et al., 1993**).

The route of administration of misoprostol was noted to be a significant factor, whereas multiple studies indicated that vaginal misoprostol was more effective than oral misoprostol even with equivalent doses. There has, however, been the worry of excessive uterine contractility with vaginal doses of 50 mcg or higher (**ACOG Committee Opinion, 2000 & 1999**).

AIM OF THE WORK

To assess the risk for emergency cesarean section between nulliparous and multiparous women who will undergo induction of labor in gestational weeks ≥ 41 and to evaluate if parity and Bishop score affected this association.

POSTTERM PREGNANCY

Definition:

The expressions postterm, postdate, postmature are often loosely used interchangeably to signify pregnancies that has exceeded duration considered to be the upper limit of normal (*Cunningham et al., 1997*).

The gestational period for a developing human embryo is usually calculated from the first day of the last menstrual period (LMP). The average expected date of delivery (EDD) is 280 days $\pm$ 14 days (40 $\pm$ 2 weeks) (*Hobart et al., 2000*).

Definition in the literature has ranged from completed 41 weeks (*Rayburn et al., 1994*) to complete 43 weeks (*Beischer et al., 1996*).

Several studies considered a pregnancy postdate at the beginning of 41 weeks from the last menstrual period (*Sacks and Freidam, 1986*).

The best name to use for a pregnancy that advances beyond 42 weeks is Postterm. The term postdatism is inadequate because there is no definition of the dates to which the term refers (*Arias et al., 2001*).

The term “Postmaturity”, “Dysmaturity” and “Placental dysfunction syndrome” all refer to a condition that result in infants with late onset wasting and manifestations of intrauterine nutritional deprivation, which are not unique to prolonged pregnancy (*Sims et al., 2001*).

The term “postmaturity syndrome” is the best expression to be used when one is referring to the postdate infant with this problem (*Sims et al., 2001*). *Arias et al. (2001)* mentioned that the prolonged terms is used to refer to those pregnancies advancing beyond the expected date of delivery or pregnancies that advance beyond 42 weeks.

Incidence:

The postterm pregnancy occurs in 2.5-12% of pregnancies depending on the method used for measurements. Most published articles agreed that 80% of births occur between 38 and 42 weeks, 3.5-14.3% occurs beyond 42 weeks and 4.4-7.3% beyond 43 weeks (*Montan et al., 2001*).

The reported frequencies from 4-14% with an average about 10%. The incidence of subsequent postterm birth increases from 10 to 27% if first birth was postterm and to 39% if there had been 2 previous successive postterm deliveries (*Bakketeig et al., 2000*).

Aetiology:

Various theories have been advocated to explain the pathogenesis of the postdate pregnancies. The actual physiologic cause responsible for prolonged pregnancy has not been yet elucidated and until the mechanisms for the initiation and maintenance of labor are defined more clearly the etiology of the postdate pregnancy will probably remain obscure (*Ahn et al., 2002*).

Fetal anencephaly was frequently associated with a postterm pregnancy. This was believed to be due to pituitary adrenal axis insufficiency. However, this should be a rare cause for a postdate pregnancy (*Ahn et al., 2002*).

Normally, fetal plasma corticosteroids levels rise prior to the onset of labor and failure to elevate plasma cortisol in the fetus contribute to prolonged pregnancy. Where intra-amniotic administration of steroids in postterm pregnancy induces labor (*Georigieff et al., 2000*).

Placental sulfatase deficiency and extrauterine pregnancy are rare conditions associated with postdate pregnancy. The former, an X-linked recessive disorder is characterized by a male fetus, low estriols and prolonged pregnancy. With estriols being used less frequently today, this disorder will probably not be diagnosed as readily (*Haddad et al., 1998*).

It is now clearly established that prostaglandins play a crucial role in the onset and maintenance of human labor. Thus, it is not unlogic that suppression of endogenous prostaglandin synthesis by prostaglandin inhibitors intake during the last 6 months of pregnancy may be resulting in delaying the onset of labor. On the other hand, there is increasing evidence that formation of prostacyclin, and possibly thromboxane, may be of vital importance for placental function and fetal well-being (*Crowley et al., 2001*).

Risk Factors:

The influence of maternal age on prolonged pregnancy had been described by many reports dating back to the sixties. Some studies found steady decrease in the incidence of postterm pregnancy with advancing age. Similar findings have been reported by other investigators (*Beischer et al., 1996*).

Many studies agreed that advancing maternal age does not appear to influence the incidence of postterm pregnancy. In the mean time, all these studies stated that their findings have been influenced by early intervention (*Bakketeig et al., 2000*).

Parity, similar to maternal age does not appear to influence the incidence of postdate pregnancy (*Ahn and Phelan, 1998*).

With maternal age held constant, prolonged pregnancies were encountered more frequently among primigravidas and women of high parity (4 or more) (*Eden et al., 2000*).

The incidence of prolonged pregnancies in multigravidas and primigravidas may vary among specific age group. Below the age of 30 years, the incidence for primigravidas is higher than multigravidas, with reversal of the incidence over the age of 30 years, and by the age of 35 years, the incidence for multigravidas is almost 4 times as compared with that for primigravidas (*Sawyer et al., 1999*).

Women who deliver a postterm infant weight are significantly more than those gravidas who deliver term infants. These results do not lend themselves to the prediction of those patients who will become postdate. The maternal weight at delivery overlap considerably, however, this difference does appear to correspond with the higher fetal and placental weights observed in these pregnancies (*Eden et al., 2000*).

Pathologic changes in postterm pregnancy:

- *The Placenta:*

Extensive study of placental development and physiology indicates that placental development is complete by the fifth month of gestation. From this point on, there are minor modifications to ensure adequate nutritional and oxygen supply to the growing fetus. It appears that peak placental function is achieved at approximately 36 weeks of gestation, after which diminishing function is a normal process (*Campbell et al., 1988*).

By the end of the first half of pregnancy, the fetoplacental index is 3:1 increasing to 6:1 at the time of parturition. These ratios are also characteristic of postterm pregnancy. Diminution of placental function during the last month of pregnancy may be exaggerated by mother's abnormalities such as cardiovascular and kidney diseases, fetal disorder such as infection and malformations factors associated with the uterine status such as hypertonus and anomalies of the placenta such as hypoplasia and infarcts as well as postterm pregnancy (*Chernukha et al., 1998*).

Microscopic changes of the placenta in women with postterm pregnancy are characterized by sclerosing of the stroma of villi and vessels, excessive deposition of fibrinoid masses in the intervillous spaces and in the stroma of the villi per se, circulatory disturbances, the development of edema and hemorrhagic foci, obliteration of vessels, the development of infarcts, extensive sites of calcification, syncytium dystrophy and lipid degeneration of the decidual cells (**Rushton, 1991**).

The content of potassium in the placenta of women with post term gestation falls by half and that of sodium goes down even more sharply. So long, potassium and sodium electrolytes play a significant role in the contractile activity of the uterus, it may be assumed that the above changes somewhat inhibit the timely development of labor. The developing placental insufficiency leads to a decrease in the viability of the fetus which affects placental function, an increase in erythroblastosis of the peripheral blood, polyglobulin and a higher amount of hemoglobin, higher frequency of metabolic acidosis, impaired water exchange between the mother and the fetus and fetal distress, all are explained by placental insufficiency (**Koppelaar et al., 1998**).

Growth retardation subsequent to postmaturity is the result of uteroplacental insufficiency from a small, aging deteriorating placenta (**Rayburn et al., 1997**).

First the placenta deprives the fetus of support from anabolic processes; fetal weight is reduced as do the fetal energy stores in the adipose tissue and liver. Diminished fetal plasma volume leads to olighydramnios. With further deterioration, the placenta loses respiratory function, and the fetus faces asphyxial damage with possible stillbirth (**Fowkkes et al., 1999**).

Placental dysfunction is an important factor that complicates a prolonged pregnancy and increases the risk to the fetus, depending on the cause of placental insufficiency and the rate at which it develops, one may see different effects on the infant (**Ribbert et al., 1993**).

- ***Amniotic Fluid Volume:***

Amniotic fluid volume increases progressively during pregnancy. It is widely accepted that amniotic volume decreases more sharply as gestational age advances beyond term (**Alley et al., 1998**).

The extent of this decrease varied over several reports; early studies estimated an average decline of 31% to 35% each week; with a decrease of approximately 28% per week between 41-43 weeks. Many studies reported a decline of 12%-25% of amniotic fluid volume per week (**Marks et al., 1999**).

The decline in amniotic fluid has an impact on fetal movement in the potentially compromised fetus. There appears to be an inverse relationship between the quantity of amniotic fluid and the presence of normal fetal activity. There was a three fold to

five fold increase in sonographic evidence of oligohydramnios in patients who were presented with the complaint of decreased fetal movement. Thus, a decreased fetal movements does represent a sign of potential fetal jeopardy that appears to be related to the presence of oligohydramnios. Therefore, a decline in fetal movement should not be disregarded because the decline in fetal activity may be the sole manifestation of a decline in amniotic fluid volume (**Nelson, 1993**).

Fetal heart rate patterns are also affected by the changes in amniotic volume; there is an inverse relationship between the amniotic fluid volume and fetal heart rate deceleration on the non stress test. With reinfusion of the amniotic fluid, the decelerations disappeared. Postterm pregnancies with oligohydramnios are associated with a decrease in the renal blood flow (**Veille et al., 1999**).

Intra-partum fetal distress detected with electronic monitoring of postterm pregnancies was found not to be associated with late deceleration characteristic of utero-placental insufficiency. These observations are consistent with cord compression as the proximate cause of fetal distress (**Bochner et al., 1987**).

Although amniotic fluid dynamics are not completely understood in human beings, it is known that fetal urination and swallowing play an important role in regulation of volume. However, other regulatory factors are also considered important in the maintenance of amniotic fluid volume (**Trimmer et al., 1988**).

Measuring hourly fetal urine production using sequential ultrasonic bladder volume measurement in postdates pregnancies, diminished urine was found to be associated with oligohydramnios (*Trimmer et al., 1998*).

Several studies concluded that the pathophysiology of fetal distress and perinatal morbidity in postterm gestation is due to oligohydramnios that leads to umbilical cord compression, rather than placental dysfunction. This finding has been supported by the fact that postdate pregnancies associated with normal amniotic fluid volumes have been found to be lower risk for fetal compromise (*Cardozo, 1995*).

Complications of Postterm Pregnancy:

The incidence of obstetric and neonatal problems increases in pregnancies past 280 days of gestation, for each week of gestation after 40 weeks the incidence of these complication increases significantly, in addition to the neonatal complications there are maternal anxiety and emotional disturbances that may be exacerbated by poor counseling (*Ohel et al., 1995*).

- *Macrosomia:*

Although several definitions of macrosomia are used in English literature, the most commonly used and most widely accepted is the infant whose birth weight is >4000 grams. The postdate fetus should continue to grow, although at a reduced

rate, in the absence of utero-placental insufficiency. Thus, an otherwise healthy infant may become macrosomic with continuation of pregnancy. The incidence of macrosomia is 3 to 7 folds more than in term deliveries (*Pollack et al., 1997*).

The primary maternal risk is caesarean section, with its increased incidence of postpartum infection, hemorrhage, prolonged hospitalization, wound complications, and pulmonary emboli. The cesarean section rate is more than double when passing the forty-second week compared to gestation at 38 to 40 weeks. This is attributed primarily to the incidence of cephalopelvic disproportion resulting from large infants (*Hirata et al., 1990*).

One of the most serious complications associated with postterm pregnancy is shoulder dystocia in which the infant's head has been delivered and there is difficulty or inability to deliver the shoulders (*Hopewood et al., 1982*).

- ***Meconium Aspiration Syndrome (MAS):***

During the postdate period the amniotic fluid volume decrease more or less progressively after 40 weeks of gestation. When oligohydramnios is present in postdate pregnancy, there is a significantly greater likelihood of meconium staining of amniotic fluid. Postterm fetuses may be at higher risk of meconium aspiration in utero (*Montan et al., 2001*).

Prepartum meconium aspiration is the potential danger of

postdate pregnancies. Meconium staining of amniotic fluid serves as a primary ingredient in the lower Apgar score and higher incidence of meconium aspiration syndrome and fetal distress encountered in the postdate group (**Boisselier et al., 2001**).

There are two-fold increase in meconium release, and eight fold increase in meconium aspiration in postterm pregnancy, that is to say that not only meconium is present more often in the amniotic fluid of postterm pregnancies, but when present, it is more often aspirated. Meconium aspiration is the cause of pneumonia and significant respiratory distress and may lead to death because it doesn't only cause mechanical obstruction, but also causes chemical pneumonitis (**Naren and Philip, 1995**).

- ***Perinatal Mortality:***

All components of perinatal mortality including antepartum, intrapartum and neonatal deaths were increased at 42 weeks and beyond (**Cunningham et al., 1997**).

The higher perinatal mortality rate is due to asphyxia, birth injury and neonatal pulmonary conditions (**Goldenberg et al., 1989**).

Postterm pregnancy is associated with an increased risk of intrapartum and neonatal death rather than antepartum death. In other words, the risk associated with postterm pregnancy