INTRODUCTION

Prolonged, post-term and post-dates' are different expressions used to signify a pregnancy that has extended beyond a certain duration accepted as the upper limit of normal. This definition varies from 41 to 43 weeks of gestation. Many studies investigating management options, include 41 completed weeks of gestation ***(Siozos and Stanley, 2005)***.

A proximately 5 to 10 percent of pregnancies are post-term. Studies have shown a reduction in the number of pregnancies considered post-term when early ultrasound dating is performed. Maternal and fetal risks increase with increase gestational age, but the management of otherwise low-risk prolonged pregnancies is controversial. Antenatal surveillance with fetal kick counts, non stress testing, amniotic fluid index measurement, and biophysical profiles are used, although no data show that monitoring improves the outcome. Studies show a reduction in the rate of cesarean deliveries and possibly in neonatal mortality with a policy of routine labor induction at 41 weeks gestation ***(Briscoe et al., 2005)***.

There's a need for an objective laboratory or clinical tool to assess the status of the cervix and predict the success of labor induction ***(Dogany et al., 2004)***.

It was found that the ripe or mature cervix, as reflected by the Bishop score, is associated with high levels of dehydroepiandrosterone sulfate (DHEAS) in maternal plasma ***(Zuidema et al., 1986)***.

Dehydroepiandrosterone (DHEA) sulfate is a weak androgenic steroid produced by the adrenal cortexes of both the pregnant woman and her fetus. It acts as intermediary hormone in the fetoplacental production of androstenedione, testosterone, esterone and estradiol ***(Goolsby et al., 1996)***.

Dehydroepiandrosterone sulfate (DHEAS) is a measurable biochemical marker of cervical maturation. It stimulates collagenase and gelatinase production and increases the synthesis of PGE2 by human cervical tissues which leads to an increased proportion of decorin to collagen and cervix maturation. It exerts its effect on the cervix through specific binding sites (receptors) in the cellular plasma membrane of the cervical fibroblasts ***(Maradny et al., 1996)***.

AIM OF THE WORK

The aim is to study the relationship between preinduction maternal plasma levels of DHEAS and the success of labor induction in post-term pregnancy.

POSTTERM PREGNANCY

In 1902, Ballantyne questioned the ability of the placenta to support the fetus that "has stayed too long in intrauterine surroundings". Ballantyne further stated that the postmature infant "has remained so long in utero that his difficulty is to be born with safety to himself and his mother" ***(Ballantyne, 1902)***. By the 1950s, the syndrome was well recognized in the literature from Western Europe, where the condition was a frequent reason for induction of labor. In 1954, Clifford recognized that prolonged pregnancy could result in fetal growth restriction when he described the "postmaturity with placental dysfunction syndrome" Clifford, suggested that these neonates appeared malnourished due to recent weight loss with loose, peeling skin and meconium staining, birth asphyxia, meconium aspiration, and perinatel death were reported in severe cases ***(Clifford, 1954)***.

Prolonged pregnancy is a real problem in modern obstetrics. It causes anxiety and distress for many women, their families and obstetricians. For many women who are eagerly awaiting the birth of their child, emotional or even psychological disturbances may be encountered if delivery does not occur at or soon after estimated date of delivery. This may be exacerbated by poor counseling ***(Saunders and Paterson, 1991)***.

DEFINITIONS:

The terms postmature, postdates, postterm and prolonged pregnancy are often loosely used interchangeably to signify pregnancies that have exceeded a duration considered to be the upper limit of normal. Imprecision in their use, along with varying definitions of the upper limit of normal pregnancy, make a search of the literature on postterm pregnancy bewildering ***(Cunningham et al., 2005)***. Although all these terms were officially accepted by the World Health Organization (1994), post mature should be used to describe the infant with recognizable clinical features indicating a pathologically prolonged, while postdates probably should be abandoned, because the real issue in many postterm pregnancies is "post what dates?". Therefore, postterm or prolonged pregnancies are the preferred expressions for extended pregnancies ***(Alexander et al., 2000)***. It is important to note that of these postterm pregnancies, postmaturity occurs in only approximately 20-43% ***(Sims and Walther, 1989)***.

The standard internationally recommended definition of prolonged pregnancy, endorsed by the American College of Obstetricians and Gynecologists (1997), is 41 completed weeks or more from the first day of the last menstrual period (LMP), assuming valid dates and a regular 28-day cycle ***(Crowly, 2001)***.

It is important to emphasize the phrase (42 completed weeks). Pregnancies between 41 weeks 1 day and 41 weeks 6 days, although in the 42nd week, do not complete 42 weeks until the seventh day has elapsed, so ***Amersi and Grimes, (1998)*** have cautioned against use of ordinal number such as "42nd week" because of their imprecision and suggested the use of the cardinal number "42 weeks" as it refers to precisely 42 completed weeks.

INCIDENCE:

The reported incidence of pregnancies reaching 42 weeks of gestation ranges from 4% to 14%, averaging about 10%. The wide variation is a result of different definitions, induction policies and proportions of women with pregnancies of uncertain dates. Accurate assessment of gestational age by ultrasound is resulting in a reduction in the incidence of prolonged pregnancy ***(Siozos and Stanley, 2005)***. a reduction in prolonged pregnancy in New South Wales from 4.6% in 1990 to 2.8% in 1996 was reported in ***Roberts et al. (1999)*** Thus, routine ultrasound in early pregnancy appear to enable better gestational age assessment and reduces rates of induction of labor for postterm pregnancy ***(Neilson, 1999)***.

Women who have had a prolonged pregnancy have a 20% risk of recurrence in a subsequent pregnancy. Following two post-term pregnancies, the risk is higher ***(Siozos and***

Stanley, 2005). In a study with an analysis of 27,677 births to Norwegian women, it was found that, the incidence of subsequent postterm birth increased only from 10% to 27% if the first birth was postterm and to 39% if there had been two previous successive postterm deliveries ***(Bakketeig and Bergsjo, 1991)***.

Morgen and colleagues (1999) reported that prolonged pregnancy also recurred across generations in Swedish women. When mother and daughter had a prolonged pregnancy, the risk for daughter's subsequent postterm pregnancy was increased 2 to 3 folds. In another Swedish study, ***Laursen and associates (2004)*** found that maternal, but not paternal, genes influenced prolonged pregnancy. so reduced cervical nitric oxide release may be a factor ***(Vaisanen-Tommiska et al., 2004)***.

ETIOLOGY & RISK FACTORS:

Labor is a poorly defined biologic process involving fetal, placental, and maternal signals***(Norwitz et al., 1999)***.Postterm pregnancy, like many reproductive outcomes or parturition disorder, appears to have a multifactorial pathogenesis. Therefore, several risk factors for postterm pregnancy have been identified. Only a small amount of risk for postterm pregnancy is attributable to any one factor, and unfortunately, no single risk factor or combination of factors reliably predicts the outcome of

postterm pregnancy or its adverse perinatal effect ***(Stamilio, 2005a)***.

a) Maternal causes :

1 – Inaccurate dating of pregnancy:

It is clear that the most common cause of prolonged gestation is an error in determining the patient's due date. Using the LMP for the determination of gestational age is fraught with inaccuracy. Patients' failure to recall accurately the date of the first day of their LMP combined with the varying duration of the luteal and follicular phases of the menstrual cycle may result in an overestimation of gestational age. When prolongation of pregnancy is adequately documented, its cause is often undetermined and the most likely etiology is biologic variability of the duration of pregnancy ***(Smith, 1999)***.

2 – Use of some drugs during pregnancy:

Although no clear evidence exists linking prolonged nonsteroidal anti inflammatory drug therapy and post-term pregnancy, this class of drugs alters prostaglandin production and, in theory, could affect the length of pregnancy ***(Stamilio, 2005a)***.

Also a retrospective survey suggested that taking aspirin (A prostaglandin inhibitor) during the last six

months of pregnancy prolong the duration of pregnancy. However still this finding is denied by others ***(Pauerstein, 1987)***.

Maternal risk factors:

1 – Previous history of postterm pregnancy:

The recurrence risk for post-term pregnancy in patients who had a prior post-term pregnancy is estimated to be two to three times higher than baseline risk, occurring in 15% to 20% of subsequent pregnancies ***(Olesen et al., 2003)***.

2 – Maternal age:

Many studies agreed that advancing maternal age does not appear to influence the incidence of postterm pregnancy. In the mean time, all these recent studies stated that their findings have been influenced by early intervention. ***(Bakketeig and Bergsjo, 1990)***.

3 – Parity:

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

1986).

4 – Race:

In a study by ***Collins et al. (2001)*** in Children's Memorial Hospital, Chicago, it was found that African Americans and Mexican Americans have greater postterm delivery rates than do Whites; however, commonly cited individual and community-level risk factors account for most of the disparity.

b) Fetal causes:

– Congenital anomalies:

The fetus itself also plays an important part in the initiation of labor. A general characteristic of fetal endocrine maturation is the enhanced activity of the fetal hypothalamic-pituitary-adrenal (HPA) axis during late gestation. HPA axis development is associated with increased levels of adrenocorticotrophin hormone (ACTH) and adrenal corticosteroid (cortisol) in the fetal circulation, and increased corticotrophin releasing hormone (CRH) in the hypothalamus, proopiomelancortin in the pituitary, and key steroidogenic enzymes in the fetal adrenal. At term, increased levels of cortisol act on the placenta/trophoblast derived cells to increase expression of prostaglandin H synthesis (PGHS), in enhancing output of primary prostaglandins, which will stimulate uterine contractility ***(Challis et al., 2001)***.

The increase in the incidence of fetal anomalies among women who deliver beyond their due date is generally explained by abnormalities of the fetal HPA axis ***(Liggins, 2000)***. Major central nervous system (CNS) abnormalities (such as anencephaly) have long been associated with loss of the normal mechanisms that initiate labor at term. ***(Divon, 2002)***.

Also, the role of the fetal adrenal gland in the initiation of labor was high lighted by Naeye, who documented marked adrenal hypoplasia in 10 of 19 postterm fetuses with lethal congenital anomalies ***(Naeye, 1978)***.

c) Placental causes:

Additional evidence regarding the complexity of the mechanisms involved with initiation of labor is provided by the X-linked recessive deficiency of placental sulfatase, which leads to abnormally low estrogen production in affected male fetuses with a subsequent prolongation of pregnancy and difficulties in both cervical ripening and labor induction ***(Rabe et al., 1983)***.

COMPLICATIONS:

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 complications increases significantly. In addition to

the neonatal complications there are maternal anxiety and emotional disturbances ***(Ohel et al., 1995)***.

A) Fetal complications:

1 – Oligohydramnios:

Phelan et al. (1987) suggested the use of an AFI of less than or equal to 5.0 cm to define oligohydramnios as an arbitrary cut-off value based on retrospective studies. Nevertheless, it has since gained popular appeal . A vicious cycle could develop with oligohydramnios causing cord compression, resulting in further hypoxemia, oligohydramnios, and fetal heart rate **(FHR)** abnormalities. Under these circumstances, fetal hypoxemia may induce relaxation of the rectal sphincters and hence meconium staining resulting in meconium aspiration syndrome. In fact, meconium-stained amniotic fluid is found in up to 50 percent of pregnancies at 42 weeks gestation upon rupture of the membranes ***(Divon, 2002)***.

2 – Meconium stained amniotic fluid and meconium aspiration syndrome:

Meconium is a dark green viscous substance that consists of fetal intestinal epithelial cells, mucus, blood, lanugo, vernix, and gastrointestinal secretions as bile. Intestinal secretions, mucosal cells, and solid elements of swallowed amniotic fluid are the 3 major solid constituents of meconium. Water is the major liquid constituent, making

up 85-95% of meconium. It first appears in the fetal ilium between 10 and 16 weeks' gestation ***(Avery et al., 1994)***.

Passage of meconium in utero has been attributed to a fetal response to intrauterine stress ***(Fujikura and Klionsky, 1975)***. Meconium passage occurs in up to 20% of full term gestations and in more than 35% of pregnancies continuing beyond 42 weeks' gestation. Meconium passage most commonly occurs in small for gestational age and postmature fetuses ***(Steer et al., 1989)***. even in women at very low risk for obstetric complications, meconium stained amniotic fluid is common and is associated with fivefold increase in perinatal mortality compared with low risk patients with clear amniotic fluid.***(Mayman et al., 1998)***

In a study, 131 cases with intrapartum draining of meconium stained liquor were reviewed and the neonatal outcome compared to that of all deliveries during the same time. Mean Apgars were significantly lower and the proportion of neonates with poor Apgar scores was higher if thick meconium was present, but not for thin meconium. Prolonged labor was more common and associated with a particularly worse outcome in the meconium stained liquor group. CSs were performed twice as frequently, failure to progress being the indication in more than half the cases ***(Saunders, 2002)***.

Meconium aspiration syndrome is a problem to which the postterm infant is particularly predisposed. There are twofold increase in meconium release and eight-fold increase in meconium aspiration in postterm pregnancy. That is to say that not only is meconium present more often in the amniotic fluid postterm, but when present, is more often aspirated. Meconium aspiration in the alveoli can cause pneumonia and significant respiratory distress and may lead to death ***(Freeman and Lagrew, 1991)***.

Thick, and not thin, meconium stained amniotic fluid was associated with an increased risk for perinatal complications during labor and delivery. Therefore, thick meconium stained amniotic fluid should be considered a marker for possible fetal compromise, and lead to careful evaluation of fetal well being ***(Sheiner et al., 2002)***.

3 – Macrosomia:

Although several definitions of macrosomia are used in English literature, the infant, whose birth weight is > 4000 grams. The postterm 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 the pregnancy. The incidence of macrosomia is 3 to 7 folds more than in term deliveries ***(Cardozo, 1995)***.

Morbidity associated with macrosomia includes

prolonged labor, cephalohematoma and shoulder dystocia with resultant risks of neonatal bone fractures or brachial plexus palsy and forceps delivery with resultant risk of neonatal traumatic injury. There is no evidence that supports labor induction as a preventative measure for macrosomia ***(ACOG 2004)***.

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. In general, the incidence of shoulder dystocia in non diabetic women delivering an infant weighing 4 – 4.5 kg vaginally has been reported to be 10% and in infants weighing>4.5 kg 22.6%. The increase in shoulder dystociais associated with advanced gestational age and neonatal birth weight. 40% of cases of shoulder dystocia occurrs in postterm pregnancies ***(Rodriguez, 1989)***.

4 – Perinatal morbidity:

Possterm pregnancies are at significant risk for perinatal morbidity; it is 2-3 times more than in term pregnancies. The twofold greater incidence of C.Ss, with it's associated complications, is reflecting the higher rates of both fetal macrosomia and meconium stained amniotic fluid ***(Bobby and Divon, 1997)***.

The fetus or neonate of a post-term pregnancy is at