INTRODUCTION

Labor is a process through which the fetus moves from the intrauterine to the extrauterine environment. It is a clinical diagnosis defined as the initiation and perpetuation of uterine contractions with the goal of producing progressive cervical effacement and dilation. The exact mechanisms responsible for this process are currently not well understood ***(Norwitz et al., 2002).***

Induction of labor is common in obstetric practice. Most of studies reported that the rate varies from 9.5 to 33.7 percent of all pregnancies annually***(Josie and Tenore., 2003).***

Induction of labour is extensively used all over the world in cases in which continuation of pregnancy is hazardous to the mother and/or her fetus. In 2004 and 2005, one in every five deliveries in the United Kingdom was induced***(NICE., 2008).***

Over recent decades, more and more pregnant women around the world have undergone induction of labour (artificially initiated labour) to deliver their babies. In developed countries, up to 25% of all deliveries at term now involve induction of labour. In developing countries, the rates are generally lower, but in some settings they can be as high as those observed in developed countries***(WHO.,2011).***

Women who are healthy and have had an otherwise uncomplicated pregnancy may have induction of labour with

vaginal prostaglandin E_2 agents conducted on the antenatal ward, before the active phase of labor ***(Selo-Ojeme et al., 2007).***

In women with prelabour rupture of membranes at term, immediate induction of labor with PGE2 gel and expectant management followed by oxytocin result in similar low rates of neonatal infection. Immediate induction oflabor with PGE2 gel results in significanlty lower rate of cesarean section and of operative vaginal delivery in nulliparas ***(Snehamay et al., 2006).***

PGE2 increases successful vaginal delivery rates in 24 hours and cervical favourability with no increase in operative delivery rates ***(Kelly et al., 2009).***

Dinoprostone gel (PGE_2) may be used for cervical ripening for women around term who have a clinical indication for induction of labour. These agents also commonly cause labour to start ***(Hofmeyr et al., 2000).***

Oxytocin alone is very useful for induction oflabor but is not always successful, especiallyin patients with low Bishop scores***(Valadan et al., 2005).***

Sustained-released dinoprostone followed 6 hours later by an oxytocin infusion in term women with prelabour rupture of membranes was associated with a higher rate of vaginal delivery within 24 hours, and no difference in maternal-neonatal

complications was observed compared with oxytocin infusion alone***(Güngördük et al., 2012).***

Compared with spontaneous onset of labor, medical and elective induction of labor in nulliparous women at term with a single fetus in cephalic presentation is associated with an increased risk of cesarean delivery, predominantly related to an unfavorable Bishop score at admission***(Vrouenraets et al., 2005).***

AIM OF THE WORK

The aim of this study is to compare between prostaglandin E2 followed 6 hours later by oxytocin and oxytocin only in primigravidae with prelabour rupture of membranes as regards maternal and fetal risks.

PRELABOUR RUPTURE OF MEMBRANES

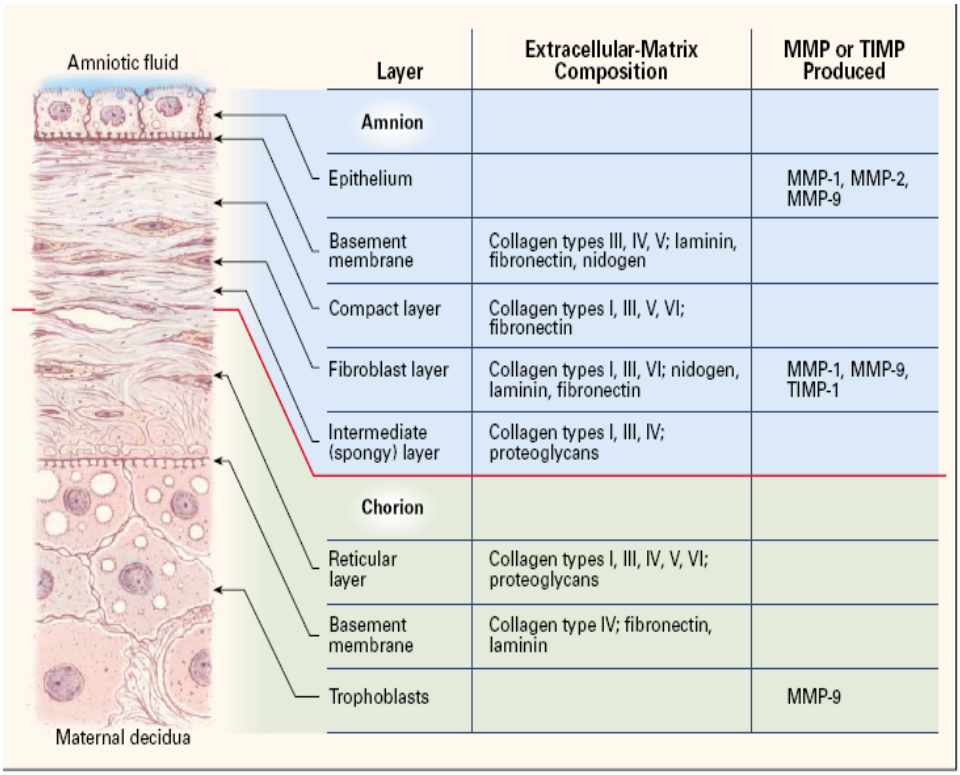
Definition:

Prelabour rupture of membranes at ter m is defined as rupture of the membranes prior to the onset of labour in women at or over 37 weeks of gestation ***(RCOG., 2007)***

Incidence:

An overall incidence of 8–10% of all pregnancies***(RCOG., 2007)***

Structure of the fetal membranes:



Layer	Extracellular-Matrix Composition	MMP or TIMP Produced
Amnion		
Epithelium		MMP-1, MMP-2, MMP-9
Basement membrane	Collagen types III, IV, V; laminin, fibronectin, nidogen	
Compact layer	Collagen types I, III, V, VI; fibronectin	
Fibroblast layer	Collagen types I, III, VI; nidogen, laminin, fibronectin	MMP-1, MMP-9, TIMP-1
Intermediate (spongy) layer	Collagen types I, III, IV; proteoglycans	
Chorion		
Reticular layer	Collagen types I, III, IV, V, VI; proteoglycans	
Basement membrane	Collagen type IV; fibronectin, laminin	
Trophoblasts		MMP-9

Fig. (1): Schematic representation of the structure of the fetal membranes at term. The extracellular-matrix composition of each layer and the production sites of matrix metalloproteinases (MMP) and tissue inhibitors of metalloproteinases (TIMP) are shown (***Samuel and Jerome, 1998).***

Clinical factors associated with rupture of the membranes

Infection

Intrauterine infection may predispose women to rupture of the fetal membranes through any of several mechanisms, each of which induces degradation of the extracellular matrix. Several organisms that are commonly present in the vaginal flora, including group B streptococci ,Staphylococcus aureus, Trichomonas vaginalis, and the microorganisms that cause bacterial vaginosis secrete proteases that can degrade collagen and weaken the fetal membranes ***(Draper et al., 1995).***

Cytokine stimulation of prostaglandin E_2production by the amnion and chorion appears to involve induction of cyclooxygenase II, the enzyme that converts arachidonic acid into prostaglandins ***(Slater et al., 1995).***

Another component of the host response to infection is the production of glucocorticoids. In most tissues the antiinflammatory action of glucocorticoids is mediated by suppression of prostaglandin production. However, in some tissues, including the amnion, glucocorticoids paradoxically stimulate prostaglandin production. Furthermore, dexamethasone reduces the synthesis of fibronectin and type III collagen in primary cultures of amniotic epithelial cells ***(Guller et al., 1995).***

Hormones

Progesterone and estradiol suppress extracellular-matrix remodeling in reproductive tissues. Both hormones

decrease concentrations of MMP-1 and MMP-3 and increase the concentrations of tissue inhibitors of metalloproteinases in the cervical fibroblasts of rabbits ***(Sato et al., 1991)***

High concentrations of progesterone decrease the production of collagenase in the cervical fibroblasts of guinea pigs, although lower concentrations of progesterone and estradiol stimulate the production of collagenase in pregnant guinea pigs ***(Rajabi et al., 1991).***

Relaxin, a protein hormone that regulates the remodeling of connective tissues, is produced locally in the decidua and placenta and reverses the inhibitory effects of estradiol and progesterone by increasing MMP-3 and MMP-9 activities in fetal membranes **(*Qin et al., 1997).***

Expression of the relaxin gene is increased before labor in human fetal membranes at term ***(Bryant-Greenwood and Yamamoto 1995)***

Programmed Cell Death

Programmed cell death, or apoptosis, has been implicated in the remodeling of various reproductive tissues, including those of the uterus and cervix. Apoptosis is characterized by the nuclear DNA fragmentation and catabolism of 28S ribosomal RNA subunits that are required for protein synthesis. In rats (which have a 21-day gestation), amniotic epithelial cells undergo apoptotic cell death as labor approaches ***(Lei et al., 1996)***.

Furthermore, in cases of chorioamnionitis, apoptotic amniotic epithelial cells are seen in conjunction with adhesive granulocytes, suggesting that the host immune response may accelerate cell death in fetal membranes ***(Leppert et al., 1996)***

Membrane Stretch and Prelabour Rupture of the Membranes

Uterine overdistention due to both polyhydramnios and multifetal gestation induces membrane stretch and rupture of the membranes. Mechanical stretching of the fetal membranes up-regulates the production of several amniotic factors, including prostaglandin $E_2$and interleukin-8. Stretch also increases MMP-1 activity within the membranes**(*Maradny et al., 1996).***

Prostaglandin E_2 increases uterine irritability, decreases synthesis of fetal-membrane collagen, and increases production of MMP-1 and MMP-3 by human fibroblasts ***(DiBattista et al., 1995)***

Most patients (90%) enter spontaneous labor within 24 hours when they experience ROM at term. The major question regarding management of these patients is whether to allow them to enter labor spontaneously or to induce labor. In large part, the management of these patients depends on their desires; however, the major maternal risk at this gestational age is intrauterine infection. The risk of intrauterine infection increases with the duration of ROM. Evidence supports the idea

that induction of labor, as opposed to expectant management, decreases the risk of chorioamnionitis without increasing the cesarean delivery rate ***(Pasquier and Bujold., 2007).***

At term, infection remains the most serious complication associated with PROM for the mother and the neonate. The risk of chorioamnionitis with term PROM has been reported to be less than 10% and to increase to 40% after 24 hours of PROM ***(Seaward et al., 1997).***

The neonatal risks of expectant management of PROM include infection, placental abruption, fetal distress, fetal restriction deformities and pulmonary hypoplasia, and fetal/neonatal death. Fetal death does occur in approximately 1% of patients with PROM after viability who have been expectantly managedand in about 1:1000 term PROM ***(Mozurkewich., 1999)***

Maternal and Fetal Surveillance

After an initial period of continuous monitoring of fetal heart rate and uterine contractions (24-48 h), if findings are suggestive of reassuring surveillance, then the patient would be a candidate for expectant management. The patient should be placed on the obstetric floor for bed rest. Because bed rest in pregnancy is associated with an increased chance of deep venous thrombosis, prophylaxis to reduce this risk should be instituted. Fetal monitoring should be performed at least once a day. If evidence of frequent cord compression is present as

determined by moderate-to-severe variables, continuous monitoring should be reinstituted. Maternal vitals need to be monitored closely. Tachycardia and fever are both suggestive of chorioamnionitis and require careful evaluation to determine the presence of intra-amniotic infections, in which case delivery and initiation of broad-spectrum antibiotics should be promptly facilitated ***(ACOG., 2007).***

Ultrasonographic examination for amniotic fluid index and fetal growth and well being should be used liberally to ensure appropriateness of continued expectant management. While oligohydramnios, defined as an amniotic fluid index of less than 2 cm, has been associated with short latency and chorioamnionitis, it alone is not an indication for delivery when other means of surveillance are reassuring. White blood cell count is not predictive of outcome and does not need to be monitored other than to support clinical suspicion of chorioamnionitis ***(ACOG., 2007).***

Digital cervical examinations should be avoided. In a noncephalic presentation, especially with a dilated cervix, continuous monitoring should be considered to avoid missing the diagnosis of cord prolapsed ***(Simhan and Canavan., 2005).***

Induction of Labour

Induction of labour (IOL) may be defined as ‘an intervention designed to initiate uterine contractions artificially

leading to progressive effacement and dilatation of the cervix and birth of the baby' ***(RCOG., 2001).***

Induction of labour should only follow informed consent by the woman.

Explain:

- Reasons for induction
- Method of induction of labour
- Potential risks
- Consequences of accepting or declining an offer of induction of labour***(RCOG., 2001)***

Women with a low cervical score (primiparous and multiparous) experience higher rates of unsuccessful induction and caesarean section ***(Enkin et al. 2000).***

In relation to spontaneous vaginal birth: 40 weeks: 58 % of women gave birth spontaneously 41 weeks: 74 % of women gave birth spontaneously, 42 weeks: 82 % of women gave birth spontaneously ***(Hilder et al. 1998).***

A policy of induction of labour before 41 weeks would generate increases in workload with no reduction in perinatal mortality' (***RCOG.,2001).***

Studies on breast (nipple) stimulation are too small to evaluate the efficacy and safety of this practice. The medical expert consensus is that breast stimulation should not be recommended as

a means of stimulating cervical ripening and or labour in high risk pregnancies ***(Kavanagh et al., 2005).***

Indications

Generally whenever continuation of the pregnancy is more hazardous for mother and / or baby than ending pregnancy.

Maternal:

- Hypertensive disorders of pregnancy
- Diabetes
- Renal disease
- Social
- Other conditions requiring the end of pregnancy
- Prelabour rupture of membranes at term

Fetal:

- Post-term pregnancy
- Intrauterine growth restriction (IUGR)
- Oligohydramnios
- Isoimmunization(***NICE.,2008).***

Methods

Several effective methods of cervical ripening and induction of labour are used for initiating labour at or around

term. Currently, medical expert consensus recommends the following:

- Sweeping the membranes
- Artificial rupture of membranes (ARM)
- Prostaglandins analogues (E1,E2)
- Intravenous oxytocin infusion

A.Sweeping the membranes

Refers to the digital separation of the fetal membranes from the lower uterine segment via vaginal examination (this is known to stimulate intrauterine prostaglandin synthesis, Research has found that sweeping the membranes reduces the duration of pregnancy and subsequent need for post-term IOL, however there is a slight increase in prelabour rupture of membranes ***(Enkin et al., 2000).***

Contraindications:

- Low lying placenta
- Planned elective caesarean

Membrane sweeping does not increase maternal or neonatal infection.

The procedure may be uncomfortable and there may be a small amount of blood loss after the procedure ***(RCOG., 2001).***

B. Artificial rupture of membranes

ARM is a surgical procedure to induce or augment labour

Indications

- Cervix is favourable
- Augmentation when labour progress is unsatisfactory due to
- inadequate contractions
- To observe the colour and amount of liquor as clinically indicated

Labour should begin within the next 12 hours and birth should within 18 hours to minimize the risk of ascending infection.

Intravenous antibiotics in labour are recommended for:

- Women with clinically suspected chorioamnionitis.
- Women with maternal Group B Streptococcal vaginal colonization (according to individual hospital criteria).
- ARM is often followed by secondary intervention with intravenous oxytocin after four hours. However, research has not identified a recommended time frame from amniotomy to secondary intervention.

(Bricker and Luckas., 2000).

Procedure:

- Abdominal examination
- The clinician identifies the cervix and membranes via vaginal digital examination

- An appropriate instrument is introduced in the vagina and the membranes are pierced (usually with an amnihook or amnicot)
- The fetal heart rate is recorded immediately following ARM and should continue to be recorded every 15 – 30 minutes until the woman is established in labour
- Once the woman is established in labour, the fetal heart rate should be recorded every 15 minutes.
- Continuous CTG if indicated.

(RCOG., 2001)