# Introduction

Induction of labour is a common obstetric procedure which is performed for a variety of medical and non medical indications ***(Schwarz et al., 2016)***.

If the cervix is unfavourable, prior ripening of the cervix makes induction of labour easier and more succeful. There are different methods for ripening of the cervix and making it ready for induction. These methods include medical methods such as the administration of prostaglandins***((Bakker et al., 2017)*** and mechanical methods such as extra amniotic saline infusion (EASI), traction on the cervix with Foley catheter and laminaria***).***

One of the methods proposed for the speeding up of the labor process (labor induction) is use of corticosteroids ***(Edwards et al., 2015)***.

Although the effects of using these substances in the labor process is not well understood, studies conducted on animals indicate the importance of the secretion of cortisol by adrenal glands in sheep fetuses and in fetuses of other animals on starting labor ***(Voutilainen and MILLER, 2016)***.

It has been observed that infusion of glucocorticoids into sheep fetuses causes premature birth induction ***(Chrousos, 2013)***.

These studies have prepared the way for bringing up the role of corticosteroids in the speeding up of labor induction in women. In studies carried out, corticosteroids have been employed using extra-amniotic and intravenous methods and in some of these studies, both methods have proved successful- ***(Kavanagh et al ., 2012)***.

Corticosteroids have been suggested for assisting in the ripening of the cervix . As the presence of the receptors for glucocorticoids on the amniotic membrane at the begining of labor enhances the hypothesis that they probably have a role in the initiation of labor ***(Kavanagh et al., 2012).***

The process of childbirth starts from the axis of the hypothalamus, the pituitary gland, and the adrenal glands. Steroid substances produced in the adrenal glands of the human fetus affect the placenta and the membranes and transform the myometrium from the static to the contractile state ***(Sato et al., 2013).***

In various studies, researchers have shown that as in sheep, the production of cortisol in the adrenal glands of human fetus affects the fetus and the membranes through increasing placental CRH production (through a feed – forward cascade) which causes the myometrium to transform from the static to the contractile state. In addition, cortisol has been proposed to affect the myometrium indirectly by stimulating the membranes to increase prostaglandin synthesis ***( Edwards et al., 2015 )***.

Furthermore, it has been revealed that the CRH derived from the placenta is an important factor in increasing maternal estrogens (especially esteriol) in the final stages of pregnancy. The resulting increase in estrogen brings about a change in the ratio of estrogen to progesterone, which promote the expression of a series of contractile proteins in the myometrium, leading to a loss of myometrial quiescence **(Hofmeyr, *2007*).**

# Aim of the Work

The aim of this work is to evaluate the effect of intramuscular administration of dexamethasone on the duration of vaginal delivery in women undergoing induction of labor.

# Chapter (1)
# Parturition

The last few hours of human pregnancy are characterized by uterine contractions that effect cervical dilatation and cause the fetus to descend through the birth canal. These forceful, painful contractions are preceded by extensive preparations in both the uterus and cervix ***(Kavanagh et al .,2012)***.

During the first 36 to 38 weeks of normal gestation, the myometrium is in a preparatory yet unresponsive state. Concurrently, the cervix begins an early stage of remodeling termed softening, yet maintains structural integrity. Following this prolonged uterine quiescence, there is a transitional phase during which myometrial unresponsiveness is suspended, and the cervix undergoes ripening, effacement, and loss of structural integrity ***(Rozenberg et al., 2005)***

The physiological processes that regulate parturition and the onset of labor continue to be defined. It is clear, however, that labor onset represents the culmination of a series of biochemical changes in the uterus and cervix. These result from endocrine and paracrine signals emanating from both mother and fetus. Their relative contributions vary between species, and it is these differences that complicate elucidation of the exact factors that regulate human parturition ***(Rozenberg et al., 2005).***

## Theories of the causes of labor

The exact mechanism, by which labor is started spontaneously, at either term or preterm, is unknown. Many theories have been proposed.

### A- Oxytocin stimulation:

Endogenously produced oxytocin, which causes uterine contractions, may play a role in the spontaneous onset of labor. Levels of oxytocin in maternal blood in early labor are higher than before the onset of labor, but there is no evidence of a sudden surge. Oxytocin influence must therefore rely on the presence of oxytocin receptors. Receptors are found in the non-pregnant uterus. There is a six fold increase in receptors at 13 to 17 weeks’ gestation and an 80-fold increase at term. The increased number of oxytocin receptors amplifies the biologic effect of oxytocin, and contractions intensity ***(YU- HSIN, 2012).***

### B-Fetal cortisol levels:

Fetal cortisol levels may influence the spontaneous onset of labor. Disruption of hypothalamic–pituitary–adrenal axis or the absence of adrenal gland or function results in prolonged gestation in humans and sheep. In sheep, infusion of cortisol or ACTH into a fetus with an intact adrenal gland causes premature labor. However, in humans, there has been no documentation of prelabor surge in fetal cortisol secretion to completely support this theory ***(Grobman et al., 2018).***

## Progesterone withdrawal:

In rabbits, the withdrawal of progesterone is followed by the prompt evacuation of the contents. In humans, there is no obvious decrease in maternal blood levels of progesterone at term or in labor. However, the progesterone level at the placental site may decrease before the onset of labor. This decrease in progesterone, in association with increased estrogen levels, is followed by increased formation of gap junctions, which permit coupling of the myometrial cells ***(YU-HSIN, 2012).***

### C- Prostaglandin release:

Prostaglandins, particularly PGF 2(alpha) and PGE2, have long been believed to be involved in the spontaneous onset of labor. The normal processes of labor appear to result in inflammation, which results in increased prostaglandin synthesis. Prostaglandins produced in myometrial tissue may contribute to the effectiveness of myometrial contractions during labor, and may soften the cervix independent of uterine activity ***(YU-HSIN, 2012).***

## Maternal–fetal interactions

In the intervillous space, the syncytiotrophoblasts release corticotropin-releasing hormone (CRH), progesterone, and estrogens into the maternal blood and into the fetal blood. Cortisol passes through a maternal artery and enters the intervillous space, where it stimulates the production of CRH by the syncytiotrophoblasts. A fetal umbilical vein carries CRH into the fetal circulation, stimulating the fetal pituitary to synthesize corticotrophin and drive fetal adrenal cortisol and dehydroepiandrosterone sulfate (DHEAS) synthesis ***(Sato et al., 2013).***

Cortisol and CRH stimulate the fetal lungs to produce surfactant protein A, which moves from the amniotic fluid to the amnion, where it stimulates the production of cyclooxygenase 2 (COX-2) and the synthesis of prostaglandin E2. They pass along the chorion and decidua and stimulate the underlying maternal myometrial cells to synthesize additional COX-2 and prostaglandin F2α ***(*****Saeideh** ***et al., 2003).***

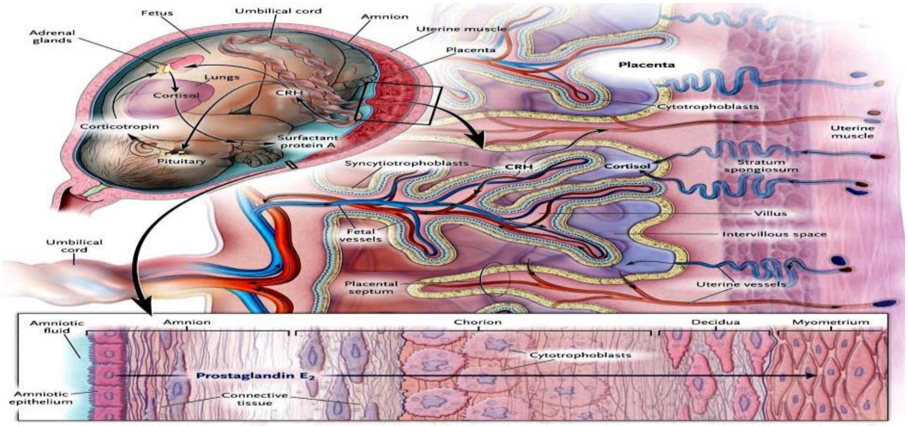


**Figure (1):** Maternal – Fetal Interactions.

## Cervical changes during prelabor and labor

The normal human cervix in the nullipara is about 2.5 cm to 3 cm in length, 2 cm to 2.5 cm in its anteroposterior diameter and 2.5 cm to 3 cm in its lateral diameter. This difference is due to the shape of the cervical canal, which is straight in the sagital plane and spindle shaped in the frontal plane. The wall of the cervix is about 1 cm thick throughout its length ***(Rev Bras, 2017).***

During pregnancy, the length of the cervix remains relatively unchanged but it varies in width by about 1 to 2 cm. The external os usually remains firmly closed up to the 15th week of pregnancy. From the 15th to 20th week it dilates in 30% of primigravidas and in 39% of multigravida. In the subsequent course of pregnancy, the external os dilates in a further number of women ***(Hernández et al., 2017)*** The internal os does not remain closed up to the full term pregnancy, it shows little dilatation from the 24th to the 28th week of pregnancy The process of connective tissue remodeling in the cervix during pregnancy occurs in four stages: softening, ripening, dilation, and repair. Although overlapping in time, each stage is uniquely regulated ***(Hernández et al., 2017).***

Although the cervix contains a small amount of smooth muscle, its major component is connective tissue. Rearrangement of this collagen- rich connective tissue is necessary to permit functions as diverse as maintenance of a pregnancy to term, dilatation to facilitate delivery, and repair following parturition so that a successful pregnancy can be repeated ***(Vahratian et al., 2016).***

Throughout pregnancy, collagen is actively synthesized. It is also continuously remodeled by collagenase, secreted from both cervical cells and neutrophils in an apparently slow and precise fashion. Collagen is degraded by collagenase both intracellularly, to remove structurally defective procollagen to prevent the formation of weak structural collagen, and extracellularly, to slowly weaken (so-called softening or ripening) the collagen matrix to allow delivery of the pregnancy ***(Read et al., 2018)***

As gestation advances, degradation and extraction of collagen from cervical tissue (a phenomenon not observed in non-pregnant state), by collagenase (now called matrix metalloproteinases) helps to maintain balance between newly synthesized collagen thus regulating total collagen concentration in the cervix ***(Saeideh et al., 2003).***

## Cervical changes During Labor:

Dilatation and effacement of the cervix during labor are not only a result of uterine contraction, but are also dependent upon ripening processes within the cervix ***(Jozwiak et al., 2012).*** The laboring cervix is histologically marked by the presence of neutrophils, and they account for a further significant increase in the level of protease found in the cervix and serum ***(Bartha et al.,2015)*** indicated that cervical ripening precedes myometrial contractions of labor by several weeks as evidenced by serial measurement of cervical length and this suggests that parturition in women is a process of long duration and that uterine contraction of labor are late events in parturition process. Before the onset of labor the cervix become softer which facilitate dilation of the cervix once forceful myomtrial contraction of labor begin. The effective force of the first stage of labor is uterine contraction, which exerts hydrostatic pressure through fetal membranes against the cervix and lower uterine segment ***(Friedman, 2001).***

As the result of the action of these forces, two fundamental changes occur effacement and dilation, for the head of the average fetus at term to pass through the cervix, the cervical canal must dilate to a diameter of about 10 cm; at this tune the cervix is fully dilated, the obliteration or taking up of the cervix is the shortening of the cervix from a length of about 2 cm to a more circular orifice with almost paper-thin edges This process is referred to as effacement and takes place from above downward ***(Friedman, 2001).***

The muscle fibers at about the level of internal os are pulled upward into the lower uterine segment, as the condition of the external os remains temporary unchanged. The edges of internal os are pulled upward several centimeters to become a part of the lower uterine segment. Effacement may be compared with a funneling process in which whole length of a narrow cylinder is converted into a very obtuse, flaring funnel with small circular orifice for an outlet ***(Friedman, 2001)***

As the result of increased myometrial activity during uterine preparation for labor, effacement of the softened cervix sometimes is accomplished before active labor begins.

Effacement causes expulsion of the mucus plug as cervical canal is shortened. Compared with the body of the uterus, the lower uterine segment and the cervix are regions of lesser resistance ***(Friedman, 2001).*** Therefore during contraction the hydrostatic pressure on amniotic sac in turns dilates the cervical canal like a wedge. The patterns of cervical dilation that takes place during the course of normal labor takes the shape of sigmoid curve, two phases of cervical dilation are the latent phase and active phase ***(Friedman, 2001).***

The onset of latent phase of labor, as defined by ***Friedman, 2001,*** is the point at which the mother perceives regular uterine contraction. The latent phase for most women ends between 3 and 5 cm of dilatation, this threshold may be clinically useful, for it defines cervical dilatation limits beyond which active labor can be expected. Also the duration of latent phase is more variable and subject to sensitive changes by extraneous factors and by sedation and myometrial stimulation ***(Friedman, 2001).***

The active phase has been divided to acceleration phase, phase of maximum slope and deceleration phase. The cervical dilatation of 3 to 5 cm or more, in the presence of uterine contractions, can be taken to reliably represent the threshold for active phase ***(Friedman, 2001).***

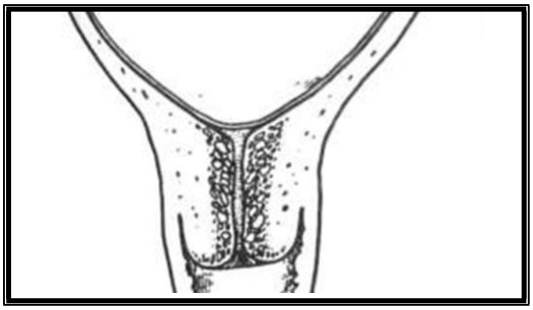

**Figure (2):** [Cervix near the end of pregnancy but before labor in primigravida] ***(Friedman, 2001).***

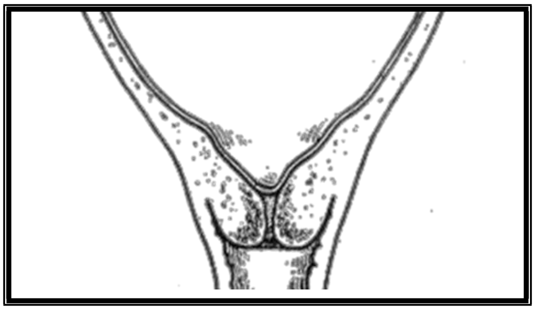

**Figure (3):** [Beginning effacement of the cervix. Note dilatation of the internal os and funnel shaped cervical canal in primigravida] ***(Friedman, 2001).***

**Figure (4):** [Further effacement of the cervix in primigravida] ***(Friedman, 2001).***

**Figure (5):** [Cervical canal obliterated that is, the cervix is completely effaced in primigravida] ***(Friedman, 2001).***

As labor begins, there are significant changes in the levels of hyaluronic acid, cytokines (interleukin-1 [beta] and interleukin-8), and collagenases that further degrade the cervical collagen. This complex interaction allows the cervix to soften and prepares it for dilation ***(Reprod et al., 2018)*** Cervical consistency ranges from firm to soft.

Cervical softening during pregnancy is a unique phase of the tissue remodeling process characterized by increased collagen solubility and maintenance of tissue strength During this process, the junction between the fetal membranes and the decidua breaks down, and an adhesive protein – fetal fibronectin – enters vaginal fluids ***(Crane, 2012)***.

This is a clinically useful predictor of imminent delivery (Smith, 2007). The normal prelabor cervical length is 3–4 cm. The cervix is said to be 50% effaced when it shortens to approximately 2 cm, and fully effaced when there is no length and it is as thin as the adjacent lower segment of the uterus. Effacement is determined by assessing the length of the cervix from the external to the internal os ***(Huber et al., 2015).***

The process of cervical effacement and dilatation differs between primigravida and multiparous patients. In the latter, effacement and dilatation are occurring simultaneously, while in the case of primigravida, effacement precedes dilatation ***(ACOG, 2016).***