COMPARATIVE STUDY OF 25µg VERSUS 50µg OF INTRAVAGINAL MISOPROSTOL FOR INDUCTION OF LABOR

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M.S. IN OBSTETRICS AND GYNAECOLOGY

BY

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APRIL- 2013

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DR. VIDYASHREE

LIST OF ABBREVIATIONS USED

PG: Prostaglandins

GIT: Gastrointestinal tract

NSAIDS: Non Steroidal Anti-inflammatory Drugs

MCP: Metalloproteinases

IL: Interleukins

PE/E: Preeclampsia/ Eclampsia

IDI: Induction delivery interval

CPD: Cephalopelvic disproportion

NICU: Neonatal intensive care unit

IUGR: Intrauterine growth restriction

GDM: Gestational diabetes mellitus

FHR: Fetal heart rate

ACOG: American College of Obstetrics and Gynecology

MSL: Meconium stained liquor

ABSTRACT

Objective: To determine and compare the efficacy and safety of 25 µg and 50µg of intravaginal misoprostol for induction of labor after 37 completed weeks of gestation and to determine the maternal and fetal outcome.

Materials and methods: This was a prospective study conducted from January 2011 to August 2012 in R.L.Jalappa Hospital and Research centre, Tamaka, Kolar. A total of 200 cases were included in the study. Each group was alternatively induced with 25µg and 50µg of intravaginal misoprostol at sixth hourly interval till the patient gets adequate uterine contractions or cervical dilatation of ≥ 3cms or a maximum of 6 doses are administered. If they do not respond to the above protocol (after receiving 6 doses of misoprostol), they were considered as failed induction and further PGE2 or oxytocin was used for delivery if required. The progress of labor was monitored by partogram in active stage of labor. Total dose of induction, induction delivery interval, mode of delivery, maternal and fetal outcome were recorded. The collected data was analyzed using student 't' test and chi-square test.

Results: Mean number of doses required was significantly less in 50µg group when compared to 25µg group (1.76±0.77 vs. 2.13±1.01, p=0.013). The mean induction delivery interval was significantly shorter in 50µg group when compared to 25µg group (12.98±4.71 vs. 16.07±6.71 hrs, p=0.001). Oxytocin augmentation was required less in 50µg group when compared to 25µg group (35.2% vs. 70.1%, p <0.001**). Cesarean section was more common in 50µg group when compared to 25µg group (29% vs. 13%, p<0.001). Meconium stained liquor was more in 50µg group compared to 25µg group (p=0.022). Maternal adverse effects were more common in 50µg group

(11% vs 30%, p=0.001). Abnormal uterine contractions were more common with higher dose. Babies with low Apgar score, requiring resuscitation and NICU care were significantly higher in 50µg group.

Conclusion: Misoprostol as a method of induction of labor intravaginally in dosage of 50µg is more efficacious than 25µg in terms of shorter induction delivery interval and less oxytocin augmentation, but it is less safe both for the mother and the fetus due to high cesarean section rate, high incidence of abnormal uterine contractions, FHR abnormalities, meconium stained liquor, low Apgar score and NICU admission.

Keywords: Misoprostol, induction of labor, meconium

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INTRODUCTION

Induction of labor is the stimulation of regular uterine contractions before the spontaneous onset of labor, using mechanical or pharmacological methods in order to generate progressive cervical dilatation and subsequent delivery. Induction of labor is indicated when the benefits to either the mother or the fetus outweigh those of continuing the pregnancy.[1]

For majority of women, labor starts spontaneously and results in vaginal delivery at or near term. However, because of medical or obstetric complications of pregnancy, labor induction is often required. This process has the potential to confer major maternal and perinatal benefits.[2]

To be successful, induction of labor must fulfill three aims:

1. It should result in adequate uterine contractions and progressive dilatation of cervix.
2. This labor should result in vaginal delivery.
3. In viable pregnancies, these aims must be achieved with minimum discomfort and risk to both mother and fetus.[3]

It has been known for years, that achievement of these goals is largely dependent upon the condition of the cervix. A “ripe”, soft, yielding cervix requires a lower quantum of uterine work than an unripe, hard and rigid one. An unripe cervix fails to dilate well in response to myometrial contractions.[4] Cervical priming methods to optimize cervical score, improve the chance of successful induction.

Induction of labor is an increasingly common obstetrical procedure and its incidence varies greatly between different countries, population groups and institutions ranging approximately from 4-40%.[5] The rate of labor induction continues to rise significantly. The reason for this increase is unclear, although it may partly reflect a

growing use of labor induction for postdated pregnancies and an increasing trend toward elective induction of labor for other indications including maternal request.[1]

Various methods have been used for induction of labor. Misoprostol is a new promising agent for labor induction. Initially it was launched for the treatment of NSAID induced gastric ulcer but it was found that it had excellent cervical ripening and uterotonic properties.[6]

Various studies have shown that misoprostol can be administered by a variety of routes and in different doses for induction of labor. Although existing evidence suggests that the 25mcg and 50mcg doses of misoprostol are currently appropriate for intravaginal administration, but further large prospective trials are required to define an optimal dosing regimen. This study is planned to compare the efficacy and safety of 25 μg versus 50 μg intravaginal misoprostol for labor induction.

OBJECTIVES OF THE STUDY

1. To determine the efficacy and safety of 25 μg of intravaginal misoprostol for induction of labor.
2. To determine the efficacy and safety of 50 μg of intravaginal misoprostol for induction of labor.
3. To compare the efficacy and safety of two regimens of vaginal misoprostol for induction of labor.
4. To determine the maternal and fetal outcome.

REVIEW OF LITERATURE

History:

The ability to induce labor has been of interest to many societies, from the primitive to the ancient to the modern. Various regimens have been developed during the course of time.[7]

An observation of the Paiute tribe described the practice of having the pregnant woman slowly decreasing her consumption of food as she approached term. The Paiute felt that if the child was slowly starved it would become anxious and try to leave the womb. The fasting was also thought to facilitate infant's passage through the birth canal because it would decrease the thickness of the maternal genitalia.[7]

Hippocrates recommended two methods. One was nipple stimulation which would lead to uterine contractions and initiation of labor. He also was the first to describe Hippocratic succession, the act of placing the patient on the tree branches and tossing, thereby hastening labor and also ensure the proper position of the fetus.[7]

In 16th century, the French obstetrician Ambrois Pare devised another instrument for mechanically dilating a woman's cervix and thus inducing labor.

In London in 1756, it was said that labor can be induced by rupturing the membranes of women with small pelvis.

In 1810, Professor James Hamilton suggested digital separation of the membranes from the lower uterine segment and then rupturing the membranes above the fetal head, ie, high rupture which gained popularity.

In 1846, Dr. Kiwisch proposed using a stream of tepid water into the vagina and against the cervix so that the water would essentially separate the surface of the fetal membranes from uterine wall.

In the 19th century and early 20th century, cervical dilatation continued to be much in vogue. Most obstetric textbooks discussed the method of digital dilatation in which two fingers were inserted into the os and then by using snapping motion, additional were inserted until it was fully dilated.[7]

In the early 20th century, ergot, quinine and pituitary extract became the primary medications for induction of labor.

In 1909, William Blair Bell started using pituitary extract to initiate and augment labor.

A few years later, Von Euler (1934-1935) and Goldblatt (1933, 1938) independently observed the smooth muscle stimulating activity of extracts of human seminal fluid.[3]

In 1949, the first modern inducing agent, oxytocin was developed by du Vigneaud who isolated pure oxytocin from the neurohypophysis and described its molecular structure.

It was Von Euler (1936) who firmly estimated that, the pharmacological effect of the active principle in human seminal fluid extracts was due to a new substance and called it "prostaglandin", in the belief that it was secreted by the prostate gland.[8] In Belgium, it was a common practice in some strata of the population to indulge in intercourse at the onset of labor in order to hasten its progress. The biological activity of seminal fluid and prostate gland has been known for many years.[8]

Among some North American tribes oral ingestion of father's semen was used to initiate when this was delayed.

However, this assumption proved incorrect when Eliasson (1959) showed that human seminal fluid prostaglandin originates from seminal vesicles. By that time the name "prostaglandin" had become firmly established.[7]

With the elucidation of its structure and synthesis by Sune Bergstrom in 1960 and discovery in 1970, that a coral (plexaura homomala) contained large amounts of prostaglandin materials that could be used for the production of pure prostaglandins, gave a boost for laboratory and clinical research.

Sultan Karim of Uganda was the first to use prostaglandins for the successful induction of labor in 1968.

In 1973, Misoprostol, a PGE_1 analogue was developed for the treatment of gastric ulcer by Searle.

In 1979, Keisse showed high level of endogenous prostaglandins in maternal circulation and amniotic fluid during labor and abortion.[9]

In 1985, when the drug came before advisory committee of the United States Food and Drug Administration, it was felt that its GIT effects were overshadowed by its abortifacient effect.

In 1987, the therapeutic potential of misoprostol as an abortifacient was clearly demonstrated in a randomized study.[9]

In 1996, Ngai et al conducted the first trial of induction of labor with oral misoprostol.[10]

In 1999, K Gemzell Danielsson et al studied the effect of oral and vaginal administration of misoprostol on uterine contractility.[11]

In 2000, Patrick S et al concluded that vaginal pH has got no effect on the efficacy of prostaglandin misoprostol for cervical ripening and labor induction.[12]

REVIEW:

Fletcher et al in 1993 in his study did a comparison between vaginal misoprostol and placebo for induction of labor in whom the cervix was unripe and delivery is indicated. He found that misoprostol was superior to the placebo in ripening the cervix and inducing labor. The change in bishop score was 5.3 in the misoprostol group compared with 1.5 in the placebo group ($p<0.001$). The mean time from insertion to delivery was 15.6 hours in the former while it was 43.2 hours in the placebo group ($p<0.001$). The need for oxytocin was also significantly less in the women receiving misoprostol compared to those with placebo (29% vs 62%, $p<0.02$). There was no difference in the two groups in terms of complications, Apgar score and mode of delivery.[13]

Kramer et al (1997) in his randomized control trial compared the efficacy and safety of misoprostol and oxytocin for induction of labor. Subjects assigned to misoprostol received 100μg in the posterior vaginal fornix every 4 hours until adequate uterine contractions were achieved. Intravenous oxytocin was started at an infusion rate of 1mU/minute and was increased by 1mU/minute every 30 minutes until adequate uterine activity was achieved. The median induction-delivery-interval was significantly shorter in the misoprostol group when compared to oxytocin (585 vs 885 minutes, $p<0.001$), the percentage of cesarean deliveries was not significantly different (23% versus 29%), although the percentage of cesarean deliveries for dystocia was lower in the misoprostol group (8 versus 21%, $p=0.02$), uterine tachysystole was significantly more common in the women receiving misoprostol (70 versus 11%, $p<0.001$) than those receiving oxytocin. There was no intergroup difference in the meconium stained liquor, 1 minute and 5 minute Apgar score.[14]

The study done by Weeks et al in 2007 on misoprostol for induction with a live fetus concluded that, when vaginal misoprostol is compared to vaginal dinoprostone, the need for oxytocin augmentation was reduced with misoprostol as there was failure to achieve vaginal delivery within 24 hours. Uterine hyperstimulation with fetal heart rate changes was variable between trials, but overall more common with misoprostol. Cesarean section rates were variable between trials, with no significant differences overall.[15]

Campbell Austin et al in their systematic review and metaanalysis (2010) compared the efficacy of dinoprostone 10mg controlled release vaginal insert with that of vaginally administered misoprostol tablets in cervical ripening and labor induction. It was found that use of the dinoprostone vaginal insert was associated with lower efficacy than vaginally administered misoprostol tablets, with regard to deliveries within 12 and 24 hours and the need for oxytocin augmentation. Both modalities had similar incidences of cesarean delivery, uterine hyperstimulation and fetal tachysystole. No significant difference in neonatal outcome was noted between the 2 groups. The safety profiles of both the drugs were similar.[16]

Sanchez-Ramos et al in 1998 reported their experience comparing 50µg of intravaginal misoprostol to the dinoprostone vaginal insert. Misoprostol treated subjects were delivered in a shorter time interval than the dinoprostone treated subjects (698 minutes vs 1041 minutes, $p< 0.001$) but incurred more tachysystole (21.3% vs 7%, $p=0.004$). No differences occurred in the route of delivery, intrapartum complications or adverse neonatal outcomes between two groups. [17]

The study conducted by Deborah A Wing et al in June 2002 on factors affecting the likelihood of successful induction after intravaginal misoprostol application for cervical ripening and labor induction. The clinical characteristics of parity, initial cervical dilatation and gestational age at entry are predictors of likelihood of success of cervical ripening and labor induction with intravaginal misoprostol.[18]

Lisa A Farah et al in 1997 did a randomized trial of two doses of Misoprostol for labor induction. Three hundred ninety- nine patients received either 25mcg or 50 mcg of misoprostol, placed intravaginally in the posterior fornix. The dose was repeated every 3 hours until adequate contractions was achieved. The induction-delivery interval was shorter in the 50 mcg group. The incidence of vaginal delivery after one dose was higher in the 50 mcg group. Patients receiving 25 mcg required oxytocin augmentation more frequently than did those receiving 50 mcg. No differences were noted in the cesarean or other operative delivery rates among patients in the two treatment groups. Although the incidence of hyperstimulation was similar between the groups, the incidence of tachysystole was higher in the 50 mcg group. They concluded that 50 mcg is associated with shorter induction to delivery interval and a higher incidence of vaginal delivery but also a high incidence of tachysystole.[19]

El-Sherbiny et al in 2001 compared the efficacy and safety of two regimens of vaginal misoprostol for induction of labor. The results were, abnormal uterine contractions were more common in Group B (50µg) compared to Group A (25µg). The induction-delivery interval was shorter with 50µg of misoprostol. Oxytocin infusion was less needed among 50µg group compared to 25µg. The cesarean section rate was 17.20% in Group A (25µg) and 14.13% in Group B (50µg). Cesarean for failed induction was

more common in Group A. Postpartum hemorrhage occurred significantly more among 50µg group. There was a trend for more neonatal complications in Group B (50µg), but this did not reach statistical significance. This study concluded that although a dose of 50 mcg misoprostol results in a significantly shorter induction-delivery interval with less need for labor augmentation, there was an increased risk of uterine contractile abnormalities and postpartum hemorrhage.[20]

Meydanli et al in 2003 did a study on labor induction with misoprostol among the post term pregnancies. Study population consisted of 120 women not in active labor. Women were randomized to receive either 25 mcg or 50 mcg until the patient exhibited three contractions in 10 minutes. There was no significant difference between the two groups with regard to the induction- delivery interval (685±201 min in the 25mcg group vs. 627±177 min in the 50 mcg group, p=0.09). The proportion of women delivering vaginally with one dose of vaginal misoprostol was significantly greater in the 50 mcg group. There were no differences in the rates of cesarean and operative vaginal delivery rates, or in the incidence of tachysystole and hyperstimulation in the two groups. Neonatal outcome were also similar.[21]

Rockhead et al in March 2003 did a comparison of two methods of labor induction with vaginal misoprostol. Misoprostol was used to induce labor in 204 consecutive pregnant women assessed as needing labor induction. 104 women were administered 100mcg of misoprostol once per 24 hours and 100 women received 50 mcg every 12 hours. In the group given 50mcg of misoprostol twice per day the mean time from insertion to delivery was significantly shorter than in the other group and the percentage of women who were delivered within 12 hrs was higher (75% vs 56.8%),

p<0.002). There was no significant difference between the two groups in the rate of cesarean births, the need for oxytocin or blood loss. There was no significant difference between the two groups in the birth weight of the neonates and in the number of neonates with Apgar less than 7 at 1 min and 5 min. There were however, significantly fewer neonates who needed resuscitation and admission to the special care nursery in the group that had received 50 mcg of misoprostol twice per day.[22]

Mutlu Meydanli et al in 2003 conducted a prospective observational study on 720 pregnant women at term with an unfavorable cervix and a medical or obstetric indication for labor induction. All patients received 50μg of intravaginal misoprostol every 4 hour upto 3 doses. A single dose of 50 mcg misoprostol was sufficient to induce labor in 612 cases (85%), whereas 108 cases (15%) received the second dose. There was a need for the third dose in a total of 62 cases (8.6%). Intravaginal misoprostol failed to induce labor in 30 cases (4.2%). 77 cases (10.6%) had meconium stained amniotic fluid. There was oxytocin requirement during labor in 92 cases (12.8%), while the mean induction- delivery interval was found to be 678.5±373.4 min. The neonatal mortality rate was nil during the study. Intravaginal misoprostol application for cervical ripening and labor induction led to an adverse outcome in a total of 98 women (13.6%). Emergency cesarean delivery was performed for non reassuring FHR tracings in 76 cases (10.6%), Logistic regression analysis revealed that the presence of tachysystole and fetal tachycardia were significant predictors of adverse outcome in women receiving 50mcg of intravaginal misoprostol for cervical ripening and labor induction.[23]

Elhassan et al in 2005 compared 25 mcg versus 50 mcg of intravaginal misoprostol for cervical ripening and labor induction. Induction- delivery interval was significantly longer in the 25 mcg vs 50 mcg group. More women in the 25 mcg group received oxytocin. Significantly fewer patients delivered vaginally in the 25 mcg group (61.3% vs 90.6%, P=0.05). There were no significant differences between the two groups in meconium stained amniotic fluid, birth weight, Apgar score and referral of the infant to the pediatrician.[24]

Cochrane Database systematic review 2010 showed that compared to placebo, misoprostol was associated with reduced failure to achieve vaginal delivery within 24 hours. Uterine hyperstimulation, without heart rate changes, was increased with misoprostol. Compared to vaginal prostaglandin E_2 and oxytocin, vaginal misoprostol was associated with less epidural analgesia use, fewer failures to achieve vaginal delivery within 24 hours and more uterine hyperstimulation. Compared to vaginal or intracervical PGE2, oxytocin augmentation was less common with misoprostol and meconium stained liquor more common. Lower doses of misoprostol compared to higher doses were associated with more need for oxytocin augmentation and less uterine hyperstimulation, with and without heart rate changes.[25]

Leo Pevzner et al in 2011 conducted a study to characterize the incidence and timing of cardiotocographic (CTG) abnormalities associated with misoprostol and dinoprostone vaginal inserts during labor induction. One thousand three hundred and eight patients were randomized to receive dinoprostone pessary, misoprostol 50 mcg (MVI 50) or 100 mcg (MVI 100) vaginal insert. 6.8% of MVI 50 treated women had a uterine contractile abnormality compared to 17.4% with dinoprostone insert and

17.3% with MVI 100 while the study drug was in situ. There was no significant difference in incidence of fetal heart rate abnormalities that occurred with the study drug – 11.2% with dinoprostone, compared to 9.9% with MVI 50 and 10.7% with MVI 100. Cardiotocographic abnormalities while the study drug was in situ occurred later in women treated with MVI 50 (7.5 hours) compared to dinoprostone (5.5 hours, p=0.003) and MVI 100 (7 hours, p=0.13).[26]

The ACOG practice bulletin recommends considering 25μg of intravaginal misoprostol as the initial dose for cervical ripening, repeated if needed not more than every 3 to 6 hour intervals. (ACOG *Obstet Gynecol*.2009). This opinion is based on the greater incidence of tachysystole noted with larger doses of misoprostol. Despite increased uterine activity with greater doses, however, greater rates of adverse maternal or perinatal outcomes have not been reported.

Although existing evidence suggests that the 25mcg and 50mcg doses of misoprostol are currently appropriate for intravaginal administration for induction of labor, but further large prospective trials are required to define an optimal dosing regimen. This study is planned to compare the efficacy and safety of 25 μg versus 50 μg intravaginal misoprostol for labor induction.

ANATOMY OF UTERINE CERVIX

The human uterine cervix is a complex organ that undergoes extensive changes during pregnancy and labor. It is the main factor responsible for keeping the fetus in utero till the end of gestation and also for its safe passage to the outside world during labor.[27, 28]

Cervix is the lowermost part of the uterus. It is cylindrical in shape and measuring 2.5-3 cm in length. It protrudes and opens into the vagina. It is divided into a supravaginal part- the part lying above the vagina and a vaginal part which lies within the vagina, each measuring 1.25 cm. It is bound at its cephalic end by the internal os and its caudal end by the external os. The cervical canal is spindle shaped and is lined by columnar epithelium. Vaginal part is covered by squamous epithelium which is continuous with that of the vagina. The mucosa is arranged in folds and has the appearance of a tree trunk with branches, hence the name 'arbor vitae'. In nulliparous, the vaginal part of the cervix is conical with the external os looking circular, whereas in parous it is cylindrical with the external os looking as a transverse slit.

Structure of the cervix:

There are three main structural components in the cervix. These are smooth muscle, collagen and connective tissue 'ground substance' containing glycosaminoglycans.

The main constituent is connective tissue which shows a typical composition of cells and extracellular substance. The cells account for 20% of the total volume. The extracellular substance consists mainly of collagen fibres, some elastin and the ground substance. The main constituent of ground substance is proteoglycans.

Extensive remodeling of the cervix occurs from early gestation which involves biochemical cascades, interaction between cellular components and extracellular matrix and infiltration of cervical stroma by inflammatory cells.

Extracellular matrix:

Collagen is predominant component of extracellular matrix. Type I collagen constitute 70% and type III 30%. They are rigid proteins present in the helical state and are cross- linked to each other, forming fibrils and bundles thus increasing their tensile strength. Peptidyl lysine oxidase is the enzyme responsible for the cross linkage and copper is a co-factor in this process. [28, 29]

Another important molecule involved in collagen structure within human cervix is presence of a small molecular weight proteoglycan, decorin. Decorin is a small dermatan sulphate proteoglycans, which coats collagen fibrils. Cervical cells secrete decorin in pregnancy. When the ratio of decorin to collagen increases, it probably causes a dispersal of collagen fibrils leading to disorganization of collagen fibers.

Elastin is another important component of extracellular matrix of the uterine cervix. They are organized parallel to and between collagen fibres. The ratio of elastin to collagen is highest at the area of internal os. Elastin in its closed status allows the uterus to retain the fetus during gestation. Any decrease in quantity and architecture of elastin has been found to be responsible for incompetent cervix.[28, 29]

Cellular component:

Smooth muscle cells and fibroblasts make up the cellular component of the human uterine cervix. The distribution of smooth muscle in the uterus and cervix vary from segment to segment. The corpus uteri is mainly a muscular organ with 70% smooth muscle, while the smooth muscle content of the cervix is about 25%,16% and 6% in the upper, middle and lower segment respectively. In humans, the cellular components undergo extensive hyperplasia in pregnancy. Changes in the connective tissue matrix and collagen are the primary factors in cervical ripening and dilatation.[28]

PHYSIOLOGY OF CERVICAL RIPENING:

Dilatation of the cervical canal from < 1cm to about 10 cm cannot be explained without involvement of biochemical changes in the main components of the cervix. In the non pregnant cervix, collagen bundles are densely and irregularly packed thus giving it a firm consistency. The histological appearance of cervix alters by 9-14 weeks of gestation[28, 29]

During pregnancy, collagen is actively synthesized and continuously remodeled by collagenase secreted by cervical cells and neutrophils. By the end of first trimester, the collagen bundles become less tightly packed due to constant degradation by collagenase with an overall decrease in collagen concentration. Also there occurs an alignment between collagen fibres along with smooth muscle cells and elastic tissue in a definite direction parallel to each other. Thus the cervix feels softer than its non pregnant counterpart. In early pregnancy, there occurs a hyperplasia of smooth muscles and fibroblasts. With the advancement of pregnancy, the cells change from a proliferative phase to a quiescent phase in which physiological cell death occurs and

decorin becomes unregulated. Decorin further suppresses cell proliferation accounting for a further increase in decorin level. Physiological cell death induces invasion of cervical stroma by neutrophils and macrophages which are in turn an important source of protease, elastase and collagenase. As the pregnancy advances closer to term, there is further decrease in collagen concentration. It is dispersed and remodeled into the fine fibres. This dispersion is aided by increase in ratio of decorin to collagen. With dispersion, the water concentration increases as hyaluronic acid, a glycosaminoglycans secreted by fibroblast increases. Hyaluronic acid has high affinity for water molecules thus further softening the cervix. [28, 29, 30]

The exact process by which the final stage of cervical ripening occurs is still unclear. Various elements involved in allowing parturition include decorin, hyaluronic acid, hormones, cytokines and protease. These factors are considered responsible for increasing the water content in the cervix, decreasing the collagen concentration and collagen restructuring.

At term as cervical cells enter physiological cell death, ratio of decorin to collagen increases, further depressing and disorganizing collagen fibrils. Also at term, the level of metalloproteinases and elastases in the cervical tissue are elevated due to increases secretion of stromal cells and by neutrophils, thus favoring degradation of collagen.
Cytokines such as interleukin-1B and interleukin 8 enhance the activity of collagenase. Interleukin 8 also appears to be a potent neutrophils chemotactic and activating factor that can stimulate extravasation and degranulation of neutrophils.

The neutrophils are a rich source of collagenases and neutrophils elastase. Matrix metalloproteinase enzymes which play a crucial role in the breakdown of number of inflammatory mediators, notably IL-8 and MCP-1 (monocyte chemotactic protein-1) have focused attention on neutrophils and monocyte recruited from the circulation as likely factors in the process. One attractive hypothesis implicates PGE2 as mainly responsible for vasodilatation of cervical capillaries and increasing their permeability to circulating neutrophils which are captured by surface adhesion molecules and drawn into the cervical stroma under the chemo attractant influence of IL-8; this chemokine is also responsible for stimulating their degranulation within the tissues to release these collagenolytic enzymes. Monocytes are also recruited into the cervix by MCP-1 and might potentially play a unifying role as a source of both PGE2 and IL-8. Hyaluronic acid has also been shown to stimulate synthesis of proteolytic enzymes by fibroblasts. The level of hyaluronic acid in cervix remains low throughout pregnancy, increases with cervical ripening and further increases dramatically with onset of labor. It has an important role in increasing water content of the cervix at term, leading to loosening and dispersal of fibres. It also has a role in neovascularization and increasing chemotactic response of neutrophils. Hormonal manipulation also has a role in cervical ripening. Estrogen stimulates collagenase production in pregnant cervix and progesterone degrades hyaluronic acid thus keeping its level low until term. Progesterone also inhibits IL-8 production by cervical tissue. Thus the effect of progesterone decreases in late pregnancy, IL-8 levels increase with production of more hyaluronic acid. [28, 29, 31]

METHODS OF INDUCTION OF LABOR: [28, 29,32]

When induction of labor is indicated and the status of the cervix is unfavorable, several methods may be used to ripen the cervix.

PHARMACOLOGICAL METHODS:

Prostaglandins (PGs):

Dinoprostone (PGE2): Currently, there are two PGE2 preparations approved by the U.S. Food and Drug Administration for cervical ripening. Prepidil contains 0.5 mg of dinoprostone in 2.5 ml of gel for intracervical administration. The dose can be repeated in 6 to 12 hours if there is inadequate cervical change and minimal uterine activity following the first dose. Cervidil is a vaginal insert containing 10 mg of dinoprostone in a timed-release formulation. The vaginal insert administers the medication at 0.3 mg/hr and may be left in place for up to 12 hours. An advantage of the vaginal insert over the gel formulation is that the insert may be removed with the onset of active labor, rupture of membranes, or the development of uterine overactivity.

Misoprostol (PGE1): Misoprostol is a synthetic prostaglandin E1 analog. The current FDA-approved use for misoprostol is for the treatment and prevention of peptic ulcer disease related to chronic non steroidal anti-inflammatory use. Administration of misoprostol for preinduction cervical ripening is considered a safe and effective "off-label" use by the ACOG. Misoprostol is inexpensive and is also stable at room temperature. Misoprostol can be administered orally or placed vaginally with few systemic side effects. Although not scored, the tablets are usually divided to provide 25 or 50 mcg doses.

Oxytocin:

Synthetic oxytocin is an effective means of labor induction. Oxytocin is most often given by intravenous infusion. It cannot be given orally because the polypeptide is degraded to small, inactive forms by gastrointestinal enzymes. The plasma half-life is short, estimated at 3 to 6 minutes, and steady-state concentrations are reached within 30 to 40 minutes of initiation or dose change. Synthetic oxytocin is generally diluted by placing 10 units in 1000 ml of an isotonic solution, such as normal saline, yielding an oxytocin concentration of 10 mU/ml. It is given by infusion pump to allow continuous, precise control of the dose administered. A common practice is to make a solution of 60 units in 1000 mL crystalloid to allow the infusion pump setting to match the dose administered (e.g., 1 mU/min equals a pump infusion rate of 1 ml/hr.

Standardized Oxytocin Regimen

1. Dilution: 10 U oxytocin in 1000 ml normal saline for resultant concentration of 10 mU oxytocin/ml

2. Infusion rate: 2 mU/min or 12 ml/hr

3. Incremental increase: 2 mU/min or 12 ml/hr every 45 minutes until contraction frequency adequate

4. Maximum dose: 16 mU/min or 96 ml/hr

Mifepristone (RU 486):

Is a competitive steroid receptor antagonist and, because of its antiprogestational action, it has been used for early pregnancy termination. It has also been studied as a potential alternative for cervical ripening and labor induction in term pregnancies.

Relaxin:

The place of relaxin as an induction or cervical priming agent is unclear, and further trials are needed to determine its place in current clinical practice.

Hyaluronic acid:

The increase in the level of hyaluronic acid is associated with an increase in tissue water content of the cervix, which is one of the mechanisms involved in cervical ripening.

NON PHARMACOLOGICAL METHODS:

Membrane sweeping:

Stripping or sweeping of the fetal membranes refers to digital separation of the chorioamniotic membrane from the wall of the cervix and lower uterine segment by inserting the examiner's finger beyond the internal cervical os and then rotating the finger circumferentially along the lower uterine segment.

Amniotomy (Artificial rupture of membrane):

Amniotomy or artificial rupture of membrane is a technique involving the perforation of the chorioamniotic membranes. It is an effective method of labor induction performed in multiparous women with favorable cervices.

Hygroscopic dilators:

Mechanical dilators placed in the lower uterine segment release endogenous prostaglandins from the fetal membranes and maternal decidua. In addition, the osmotic properties of hygroscopic dilators promote cervical ripening. These hygroscopic dilators absorb endocervical and local tissue fluids that cause swelling and allow for controlled dilation by mechanical pressure. They function by disrupting

the chorioamniotic decidual interface, causing lysosomal destruction and prostaglandin release. These events lead to active stretching of the cervix beyond the passive mechanical stretching provided by the dilator itself.

Transcervical balloon catheter:

A deflated Foley catheter, usually a 16-French 30-mL balloon, can be passed through an undilated cervix into the extra-amniotic space and then inflated. The balloon is then retracted to rest against the internal os.

INDICATIONS FOR LABOR INDUCTION: [32, 33]

Generally, labor induction is indicated when the benefits of delivery to the mother or fetus outweigh the potential risks of continuing the pregnancy. The most appropriate timing for labor induction is the point at which the maternal or perinatal benefits are greater if the pregnancy is interrupted than if the pregnancy is continued.

Absolute indications:

- Hypertensive disorders

  -Preeclampsia/eclampsia
- Maternal medical conditions

  - Diabetes mellitus

  - Renal disease

  - Chronic pulmonary disease
- Prelabor rupture of membrane
- Chorioamnionitis
- Fetal compromise

  -Fetal growth restriction

  -Isoimmunisation

  -Oligohydramnios
- Fetal demise
- Prolonged pregnancy (>42 weeks)

Relative indications:

- Hypertensive disorders

  -Chronic hypertension
- Maternal medical conditions

-Systemic lupus erythematosus

-Gestational diabetes

-Hypercoagulable disorders

-Cholestasis of pregnancy

- Polyhydramnios
- Fetal anomalies requiring specialized neonatal care
- Logistic factors

  -Risk of rapid labor

  -Distance from hospital

  -Psychological indications

- Previous stillbirth

CONTRAINDICATIONS FOR LABOR INDUCTION: [32, 33]

Generally recognized relative and absolute contraindications to labor induction are listed below.

Absolute contraindications:

- Prior classical uterine incision or transfundal uterine surgery
- Active genital herpes infection
- Placenta previa or vasa previa
- Prolapsed umbilical cord
- Transverse or oblique fetal lie
- Absolute cephalopelvic disproportion

Relative contraindications:

- Cervical carcinoma
- Funic presentation
- Breech presentation

EVALUATION BEFORE INDUCTION OF LABOR: [32]

Before inducing labor, the obstetrician should review carefully the indications for terminating the pregnancy and obtain informed consent. Assessment of gestational age and consideration of any potential risks to the mother or fetus are of paramount importance for appropriate evaluation and counseling before initiating cervical ripening or labor induction. The patient should be counseled regarding the indications for induction, the agents and methods of labor stimulation, and the possible need for repeat induction or cesarean delivery. The pediatrician should be notified to make specific plans for the care of the neonate. Maternal pelvis should be assessed as to its adequacy for vaginal delivery. Fetal weight and presentation should be determined. Monitoring of FHR and uterine contractions is recommended as for any high-risk patient in active labor.

Because of the increased risk of cesarean delivery with failed labor induction, great efforts have been made to identify predictors of the success or failure of induction and to develop interventions that may reduce these events. The favorability of the uterine cervix is one of the most significant predictors of induction success. In women undergoing elective induction of labor, there is moderate evidence that a low Bishop score. Cervical dilation is also inversely associated with cesarean delivery. In nulliparous women, a closed cervix is associated with a 50% cesarean delivery rate, whereas a 4-cm cervical dilation has a less than 10% risk of cesarean delivery.

Maternal parameters:

- Confirm indication for induction.
- Review contraindications to labor and/or vaginal delivery.
- Perform clinical pelvimetry to assess pelvic shape and adequacy of bony pelvis.

- Assess cervical condition (Bishop score)
- Review risks, benefits and alternatives of induction of labor with patient.

Fetal parameters:

- Confirm gestational age
- Assess need to document fetal lung maturity status
- Estimate fetal weight (either by clinical or ultrasound examination)
- Determine fetal presentation and lie
- Confirm fetal well-being

CERVICAL SCORING SYSTEMS:

Bishop's Score: [34]

Bishop introduced a scoring system in 1964 that takes cervical dilatation, effacement, station of the presenting part and consistency of the cervix into account.

Cervical features	**Pelvic score**			
	0	**1**	**2**	**3**
Dilatation (cm)	0	1-2	3-4	5-6
Effacement (%)	0-30%	40-60%	60-70%	≥ 80%
Station (cm)	-3	-2	-1/0	+1/+2
Consistency	Firm	Medium	Soft	-
Position	Posterior	Mid-position	Anterior	

Total score: 13 Unfavourable cervix: 0-6 Favourable cervix: 7-13

Modified Bishop's score: [35]

Calder modified the original Bishop score in 1974 which is known as Modified Bishop score and is currently used by most obstetric units. He replaced the 'effacement of cervix' denoted as percentage in the original score with 'length of cervix' in centimeters as shown below.

Cervical features	**Pelvic score**			
	0	**1**	**2**	**3**
Dilatation (cm)	0	1-2	3-4	5+
Length of cervix (cm)	3	2	1	<1
Station (cm)	-3	-2	-1/0	+1/+2
Consistency	Firm	Medium	Soft	-
Position	Posterior	Mid-position	Anterior	-

Unfavourable score: 0-5, Favourable score: 6-12

BIOCHEMISTRY OF PROSTAGLANDINS

Prostaglandins are a family of highly active, structurally similar, modified unsaturated hydroxyl fatty acids. A number of them have been identified in tissues and biological fluids and each is derived from the basic, but not itself active prostanoic acid, a cyclopentane fatty acid consisting of a five carbon ring with 2 hydrocarbon side chains attached to the neighbouring carbon atoms.[36]

Eicosanoids refer to all the 20- carbon derivatives while prostanoids indicate only those containing a structural ring. Depending upon the configuration of the 5- carbon ring each prostaglandin belongs to one of 4 groups – A,B,E and F, while for each group a suffix numeral (1,2 or 3) describes the degree of unsaturation of the side chain, thus denoting the number of double bonds each molecule contains. All the prostaglandins are hydroxylated in the 15^{th} position and possess a 13, 15 trans double bond in the lower side chain. The first cycloendoperoxides formed from 5,8,11,14 eicosatetranoic acid (arachidonic acid), following the influence of the cyclo-oxygenase enzyme systems, referred to as "the mother of all prostaglandins" are PGG2 and PGH2 with a half life of about 5 minutes.[36]

The prostaglandins of original and containing relevance to reproduction are PGE2 and PGF2 and possible PGD2- the A, B and C prostaglandins either have little biologic activity or do not exist in significant concentrations in biologic tissues. In the original work, the prostaglandin more soluble in ether was named PGE, while the one more soluble in phosphate buffer was named PGF, later, naming became alphabetical. The E and F series differ from each other in that the PGE's contain a keto-oxygen at C-9 and a hydroxyl group at C-11.[36]

The primary prostaglandins consist of these two main sets each having 3 members from all three series namely E1, E2, E3 and F1a, F2a, F3a. Prostaglandins are named A to I depending upon the structure of the five carbon ring. There are one or more double bonds in the side chains; they are expressed by the numerical subscript of PGE1, PGE2, and PGE3.[36]

MISOPROSTOL

Misoprostol (PGE1) is a methyl ester of PGE1, additionally methylated at C 16.[37,38] It was developed and marketed with US FDA's approval for the sole indication for the prevention of peptic ulcer disease caused by prostaglandins synthetase inhibitors. In the early 1990's, misoprostol has experienced increasing interest by obstetricians/ gynecologists because of its uterotonic and cervical ripening effect. The research exploiting this adverse effect has shown misoprostol to be effective in many obstetric conditions. [39, 40]

Recently, the most fascinating synthetic prostaglandin E1 analogue, Misoprostol has been focus of attention in the arena of various labor inducing agents. Clinical guidelines of the ACOG included misoprostol as an option for induction of labor, whereas the Royal College of Obstetricians and Gynecologists (RCOG) in the UK so far do not support its use for labor induction clinical trials.[39]

STRUCTURE OF MISOPROSTOL

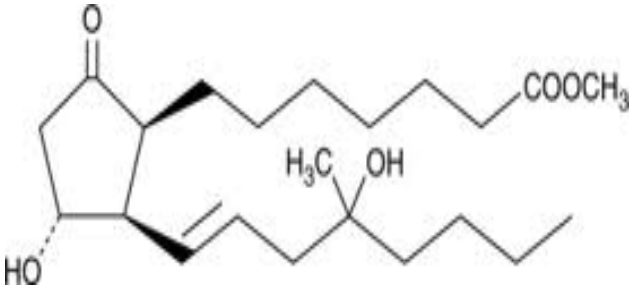


Figure 1: [36]

Misoprostol differs structurally from naturally occuring prostaglandin E1 by the presence of a methyl ester at C-1, a methyl group at C-16 and a hydroxyl group at C-16 rather than at C-15. The methyl ester at C-1 increases the anti-secretory potency and duration of action of misoprostol, whilst the movement of the hydroxyl group from C-15 to C-16 and the addition of a methyl group at C-16 improves oral activity, increases the duration of action and improves the safety profile of the drug.[36,38]

Misoprostol is metabolized by fatty acid oxidizing system present throughout the body. Renal excretion of misoprostol or its active acid metabolite is not the major pathway of elimination of active drug. Likewise, as the misoprostol oxidizing enzymes are present in several organs, its metabolism and plasma levels are unlikely to be affected in patients with hepatic impairment.[38, 39]

PHARMACOKINETICS OF MISOPROSTOL [36, 37]

Misoprostol tablets were developed to be used orally. Other routes of administration, however, including vaginal, sublingual, buccal and rectal have also been used extensively in obstetric and gynecological applications. Three pharmacological

properties, the peak concentration, time to peak concentration and the area under the serum concentration versus time curve were studied. The time to peak concentration (Tmax) represents how rapidly the drug can be absorbed; the peak concentration (Cmax) reflects how well the drug is being absorbed while the area under the serum concentration versus time curve (AUC, equivalent to bioavailability) denotes the total exposure to the drug.

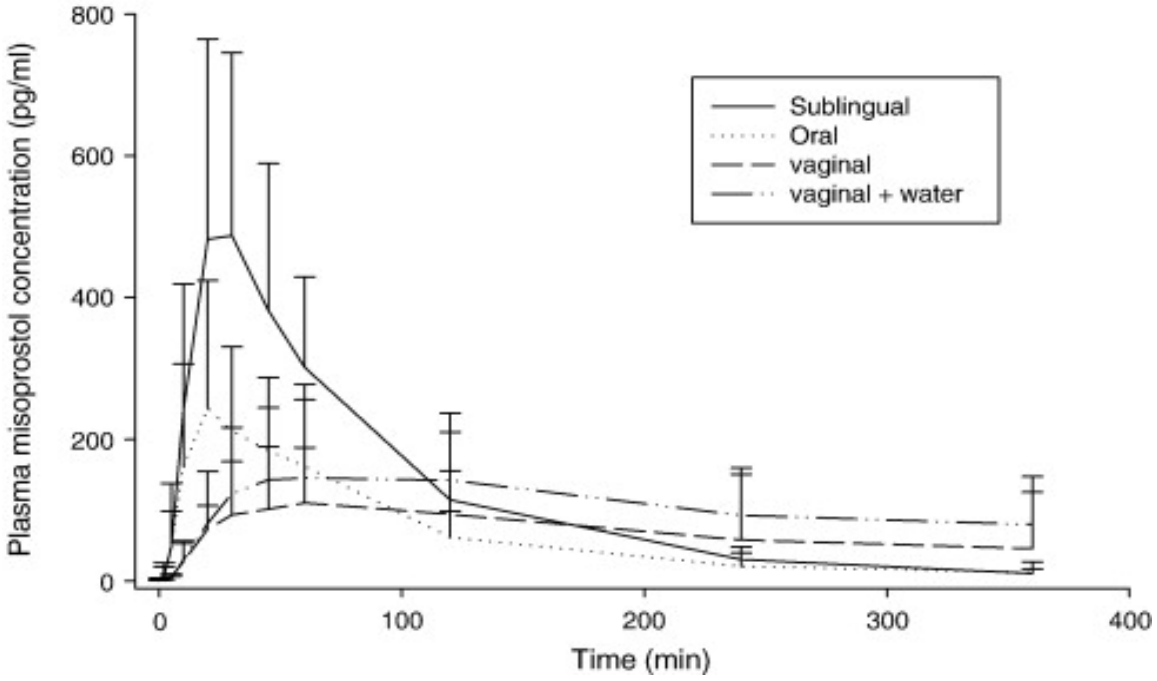


Figure 2: [37]

Oral route:

After oral administration, misoprostol is rapidly and almost completely absorbed from the gastrointestinal tract. However, the drug undergoes extensive and rapid first-pass metabolism to form misoprostol acid. With oral route of administration, onset of action is seen within 8 minutes and the duration of action lasts for approximately 2 hours.

Vaginal route:

In contrast to oral route, the plasma concentration increases gradually after vaginal administration, reaches its maximum level after 70-80 minutes before slowly declining with detectable drug levels still present after 6 hours. Onset of action is within 20 minutes and the duration of action is approximately 4 hours. Although the peak concentration after oral administration is higher than for vaginal administration, the 'area under the curve' is higher when given vaginally.

Sublingual route:

The misoprostol tablet is very soluble and can be dissolved in 20 minutes when it is put under the tongue. Sublingual misoprostol has the shortest time to peak concentration, the highest peak concentration and the greatest bioavailability when compared to other routes. The onset of action is within 11 min and the duration of action is approximately 3 hours.

Buccal route:

The drug is placed between the teeth and the cheek and allowed to absorb through the buccal mucosa. After buccal administration the Tmax is 75 minutes which is similar to that after vaginal administration, but the AUC of buccal administration is just half that of the vaginal administration.

Rectal route:

The shape of the absorption curve after rectal administration is similar to that of vaginal administration but its AUC is only 1/3 that of vaginal administration.[36]

ACTION OF MISOPROSTOL ON THE UTERUS: [37]

Administration of misoprostol results in dissolution of collagen bundles and an increase in submucosal water content of the cervix. These changes in cervical connective tissue at term by misoprostol are similar to those observed in early labor. Misoprostol is an effective myometrial stimulant of the pregnant uterus, selectively binding to EP2/ EP3 prostanoid receptors. It increases uterine tonus.

CHARACTERISTICS OF MISOPROSTOL: [36]

- It is inexpensive
- Easily stored (shelf life of 3 years)
- Is not affected by ambient temperature
- Needs no refrigeration

USES OF MISOPROSTOL: [28, 29]

Obstetrics:

- Induction of labor
- Labor induction in case of intrauterine death
- Abortion induction in cases of second and early third trimester of pregnancy associated with fetal anomalies.
- Management of missed abortion
- Medical abortion: alone or in combination with Mifepristone
- Cervical priming prior to surgical abortion: trimester I and II
- Management of atonic postpartum hemorrhage.

Gynecology:

- Cervical ripening prior to dilatation and curettage.

- Cervical ripening prior to hysteroscopy.

CONTRAINDICATIONS FOR THE USE OF MISOPROSTOL:

- Previous cesarean delivery or any other scar on the uterus
- History of asthma, glaucoma, cardiac disease
- Any hypersensitivity to the use of prostaglandins

SIDE EFFECTS OF MISOPROSTOL: [28, 29.38]

Diarrhea is the most common side effect associated with misoprostol in clinical trials; occurred in one tenth of patients. It is usually mild and self-limiting.

Other adverse effects like nausea, vomiting, abdominal pain, chills, shivering, hyperthermia may occur which are dose dependant.

Higher incidence of uterine hyperstimulation: Systematic review has found that vaginal misoprostol used to be associated with more uterine hyperstimulation with non-reassuring fetal heart rate changes than with PGE2.

Higher incidence of meconium stained amniotic fluid: Use of misoprostol is associated with increased incidence of meconium passage in labor, which may be a fetal response to uterine hyperstimulation or a direct effect of absorbed misoprostol metabolite on the fetal gastrointestinal tract.

Risk of uterine rupture: Rupture of uterus with or without a previous scar is most serious issue. There are several reports indicating increased chances of scar rupture, but total number in the trials are too small to resolve the issue. Dose relations have been implicated. [41]

Moebius syndrome: a congenital defect characterized by equinovarous, facial nerve defects, arthrogryposis and terminal limb defects have been reported in women who ingested misoprostol in first trimester. [42]

Uterine tachysystole: is defined as six or more contractions in a 10 minute period.[28]

Uterine hypertonus: is defined as a single contraction lasting longer than 2 minutes.[28]

Uterine hyperstimulation: when either condition leads to a non reassuring fetal heart rate pattern.[28]

MATERIALS AND METHODS

Source of data:

An 18 month study of pregnant women (completed 37 weeks or more) requiring induction of labor for any medical or obstetric indication, admitted to R.L.Jalappa Hospital and Research centre, Tamaka, Kolar, during January 2011 to August 2012.

INCLUSION CRITERIA

1. Woman with singleton pregnancy completed 37 weeks and beyond
2. Vertex presentation
3. Intact membranes
4. Reactive non stress test

EXCLUSION CRITERIA

1. Favourable cervix i.e. Modified Bishop score ≥6
2. Previous cesarean delivery or any other uterine surgery
3. Gravida ≥ 5
4. Any contraindication for vaginal delivery
5. Contraindication to the use of prostaglandins.ie. women with history of asthma, glaucoma, cardiac disease or any hypersensitivity to the use of prostaglandins

Written informed consent was obtained from each woman before participation.

METHOD OF COLLECTION OF DATA

It was a prospective study conducted in the Department of Obstetrics and Gynecology attached to Sri Devaraj Urs Medical College, Tamaka, Kolar from January 2011 to August 2012.

A complete history including maternal age, parity, gestational age and indication for induction of labor were noted. Abdominal examination was done to know the presentation, uterine tone and the fetal heart rate. Per vaginal examination was done to know the modified Bishop score and to rule out cephalopelvic disproportion. Cardiotocograph (CTG) and Obstetric scan were done to all the patients to ascertain the fetal well being. An informed written consent was taken prior to induction. Following exclusion of uterine contractions or a non reassuring CTG and confirmation of Modified Bishop score ≤ 5, patients received intravaginal misoprostol either 25µg (Group A) or 50µg (Group B), allotted alternatively.

The misoprostol tablet was placed intravaginally in the posterior fornix and the dose was repeated every 6 hrs till the patient gets adequate uterine contractions (3 contractions in 10 minutes) or cervical dilatation of $\geq$ 3cms or a maximum of 6 doses were administered. If they did not respond to the above protocol (even after receiving 6 doses of misoprostol), they were considered as failed induction and further PGE2 or oxytocin was used for delivery if required.

The progress of labor was monitored by partogram in active stage of labor. Patients were monitored for the fetal heart rate, uterine contractions and looked for any abnormal uterine contractions. Labor was augmented with oxytocin if required.

Total dose of induction, induction delivery interval, mode of delivery, oxytocin requirement, maternal side effects and fetal outcome like meconium stained liquor, FHR abnormalities, Apgar score, neonatal resuscitation and NICU admission were recorded.

Descriptive and inferential statistical analysis has been carried out in the present study. Student‘t’ test has been used to find the significance of study parameters on continuous scale between two groups on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

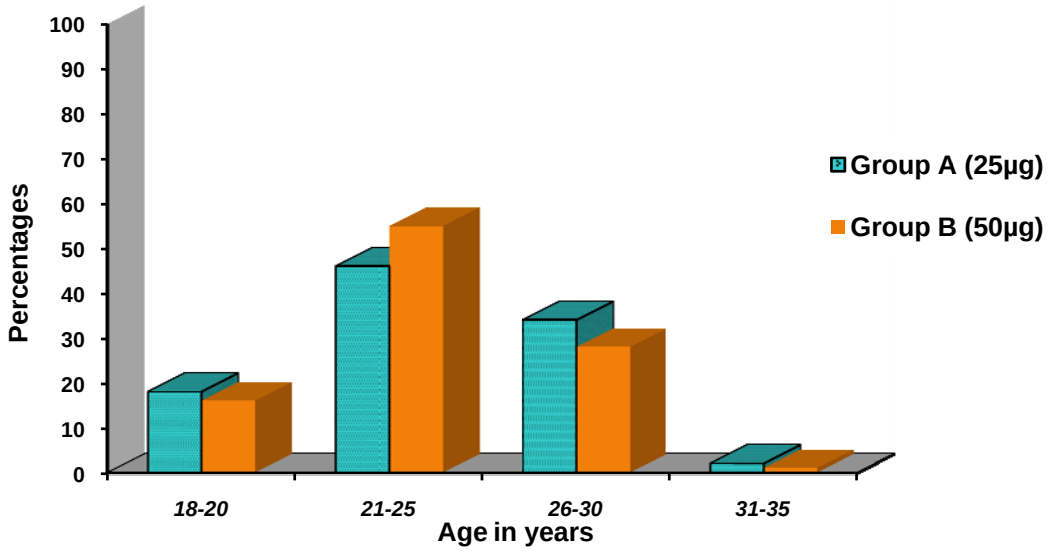
The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs and tables .

RESULTS

Table 1: Age distribution

Age in years	Group A (25µg) (N=100)		Group B (50µg) (N=100)	
	No	%	No	%
18-20	18	18.0	16	16.0
21-25	46	46.0	55	55.0
26-30	34	34.0	28	28.0
31-35	2	2.0	1	1.0
Mean ± SD	24.45±3.39		23.86±3.17	

The mean age in group A (25µg) was 24.45±3.39 years and in group B (50µg) was 23.86±3.17 years which is statistically similar with p value of 0.206.

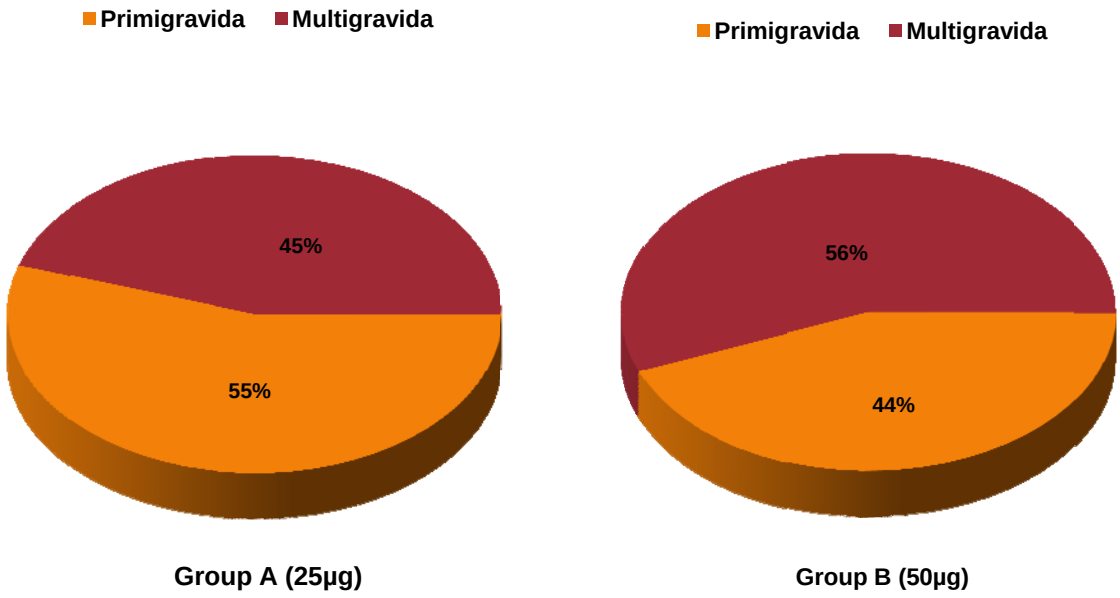


Graph 1: Age distribution

Table 2: Parity distribution

Parity	Group A (25µg) (N=100)		Group B (50µg) (N=100)	
	No	%	No	%
Primigravida	55	55.0	44	44.0
Multigravida	45	45.0	56	56.0

In group A (25µg), there were 55 (55%) primigravida and 45 (45%) multigravida. In group B (50µg), there were 44 (44%) primigravida and 56 (56%) multigravida. The parity distribution was statistically similar in two groups with P=0.120.

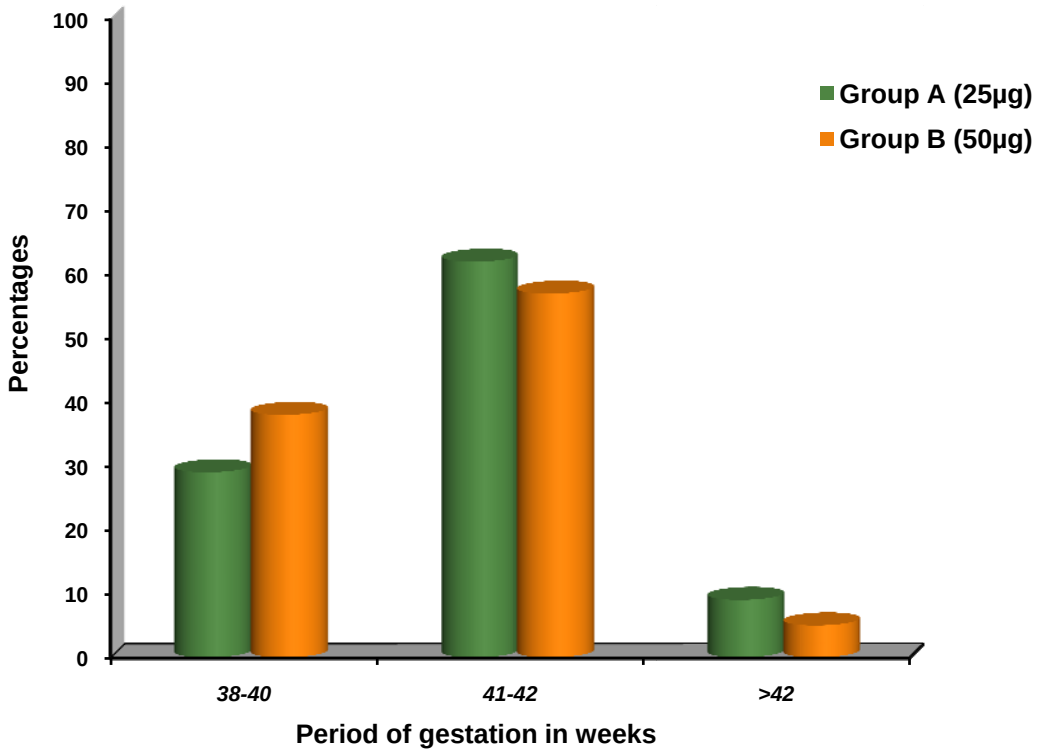


Graph 2: Parity distribution

Table 3: Period of gestation

Period of gestation in weeks	Group A (25µg) (N=100)		Group B (50µg) (N=100)	
	No	%	No	%
38 - 40	29	29.0	38	38.0
41 - 42	62	62.0	57	57.0
>42	9	9.0	5	5.0

Period of gestation was statistically similar in two groups with P=0.278

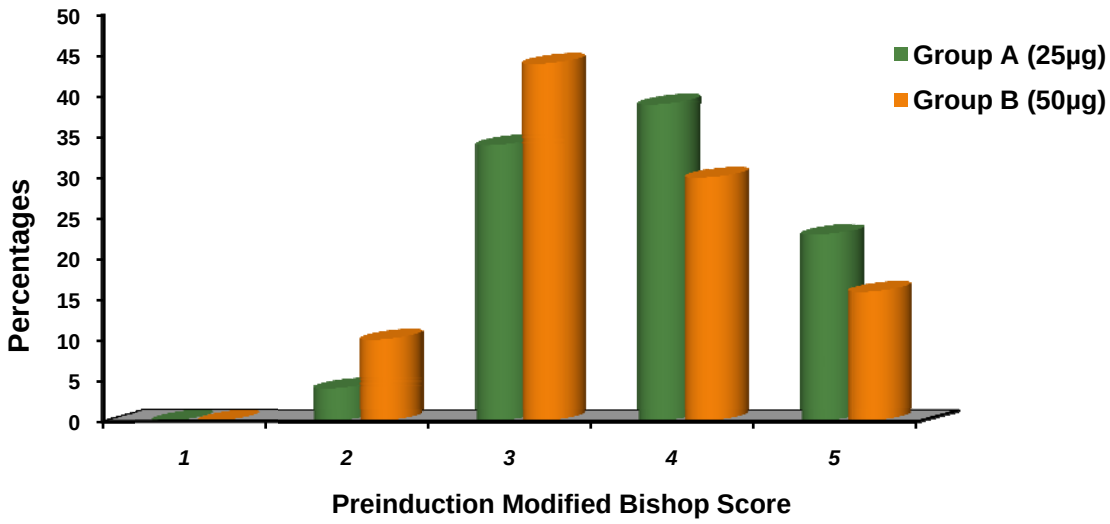


Graph 3: Gestational age

Table 4: Pre-induction Modified Bishop Score

Pre-induction Modified Bishop Score	Group A (25µg) (N=100)		Group B (50µg) (N=100)	
	No	%	No	%
1	-	-	-	-
2	4	4.0	10	10.0
3	34	34.0	44	44.0
4	39	39.0	30	30.0
5	23	23.0	16	16.0

The mean pre-induction modified bishop score in group A (25µg) was 3.81±0.84 and in group B (50µg) was 3.62±0.88 with p value of 1.000, which was statistically similar in two groups.



Graph 4: Pre-induction modified bishop score

Table 5: Comparison of maternal demographic characteristics in two groups

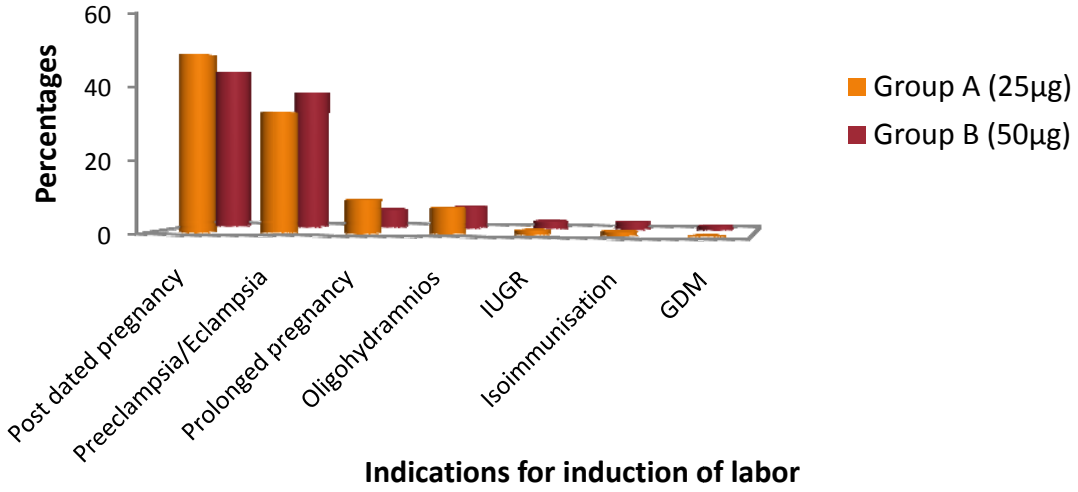
Maternal demographic characteristics	Group A (25µg) (n=100)	Group B (50µg) (n=100)	P value
Age in years	24.45±3.39	23.86±3.17	0.206
Parity			
Nullipara	55(55.0%)	44(44.0%)	0.120
Multipara	45(45.0%)	56(56.0%)	
Gestational age	40.12±1.12	39.94±1.03	0.239
Pre-induction modified bishop score (mean±S.D)	3.81±0.84	3.62±0.88	1.000

This table shows the demographic characteristics of group A (25µg) and group B (50µg). Age, parity, gestational age and the pre-induction modified bishop score all were statistically similar in both the groups.

Table 6: Indication for induction of labor

Indication for induction of labor	Group A (25µg) (n=100)		Group B (50µg) (n=100)	
	No	%	No	%
Post dated pregnancy	49	49.0	45	45.0
Pre-eclampsia/ Eclampsia	33	33.0	39	39.0
Prolonged pregnancy	9	9.0	5	5.0
Oligohydramnios	7	7.0	6	6.0
Intrauterine growth restriction	1	1.0	2	2.0
Isoimmunisation	1	1.0	2	2.0
Gestational diabetes mellitus	0	0	1	1.0

The most common indications for induction of labor in bothgroups were post-dated pregnancy and pre-eclampsia/eclampsia which was statistically similar in two groups with P=0.783.



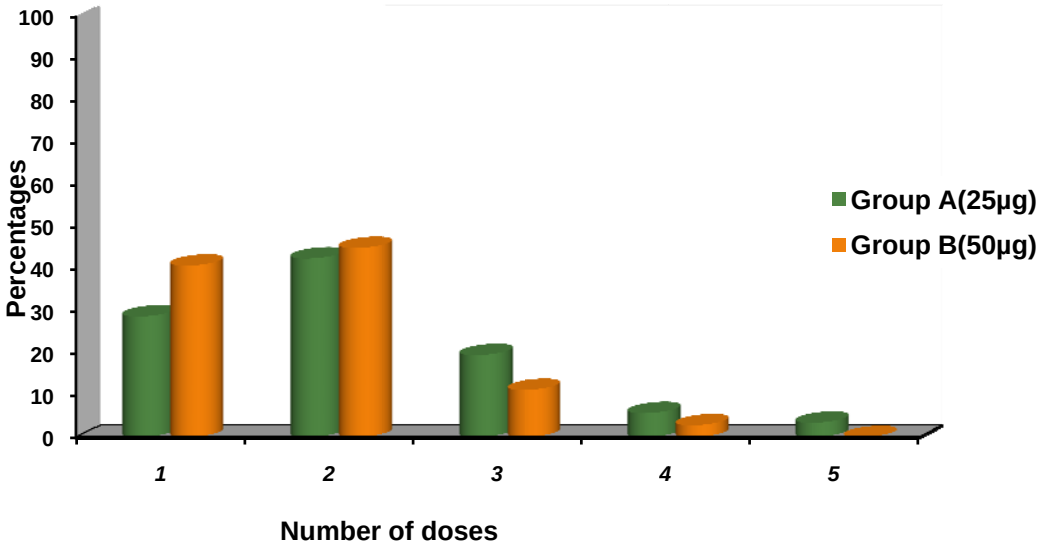
Graph 5: Indications for induction of labor

Table 7: Total number of doses used for induction

Number of doses	Group A (25µg) (n=87)		Group B (50µg) (n=71)	
	No	%	No	%
1	25	28.7	29	40.8
2	37	42.5	32	45.0
3	17	19.5	8	11.2
4	5	5.7	2	2.8
5	3	3.4	0	0.0
Mean ± SD	2.13±1.01		1.76±0.77	

In group B (50µg) 29 (40.8%) cases delivered with one dose of 50µg misoprostol. Whereas in group A (25µg) only 25(28.7%) cases delivered with one dose of 25µg of misoprostol. The p value was 0.110.

The mean number of doses of misoprostol in group A (25µg) was 2.13±1.01 whereas in group B (50µg) was 1.76±0.77 which is moderately significant (p=0.013*).



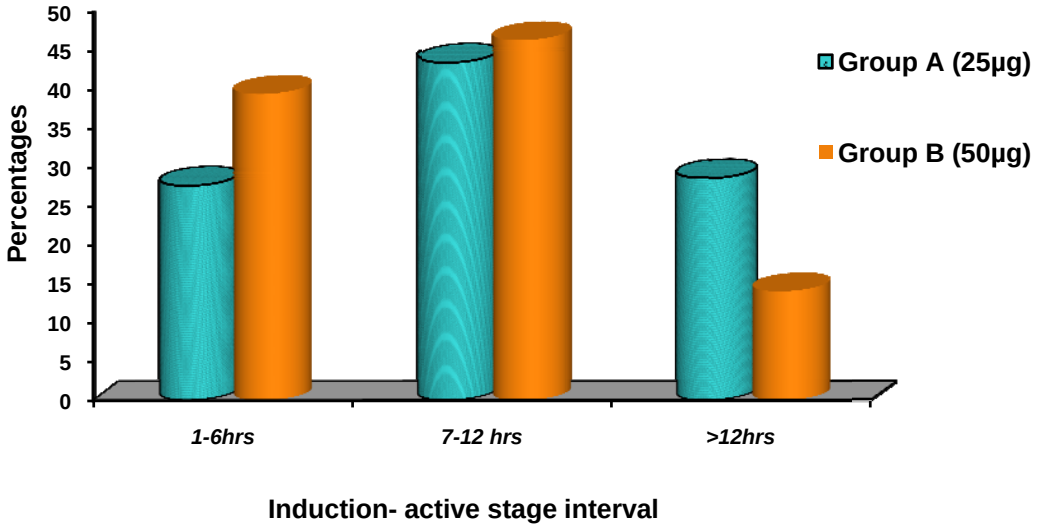
Graph 6: Number of doses required in each group

Table 8: Induction to active stage interval in vaginally delivered cases

Induction to active stage (hours)	Group A (25µg) (n=87)		Group B (50µg) (n=71)	
	No	%	No	%
1-6	24	27.6	28	39.4
7-12	38	43.6	33	46.5
>12	25	28.7	10	14.1
Mean ± SD	10.78±5.97		8.32±4.27	
Inference	Mean induction to active stage interval was significantly less in Group B (8.32 hrs) when compared to Group A(10.78 hrs) with P=0.004**			

** strongly significant

This table shows the interval between induction to active stage of labor in vaginally delivered cases.



Graph 7: Induction to active stage interval

39.4% (28/71) in group B (50µg) went into active stage of labor within 6 hours of induction whereas in group A (25µg) only 27.6% (24/87) went into active labor within 6 hours. The mean induction to active stage interval was significantly less in Group B (8.32±4.27hrs) when compared to Group A (10.78±5.97 hrs) with P=0.004**

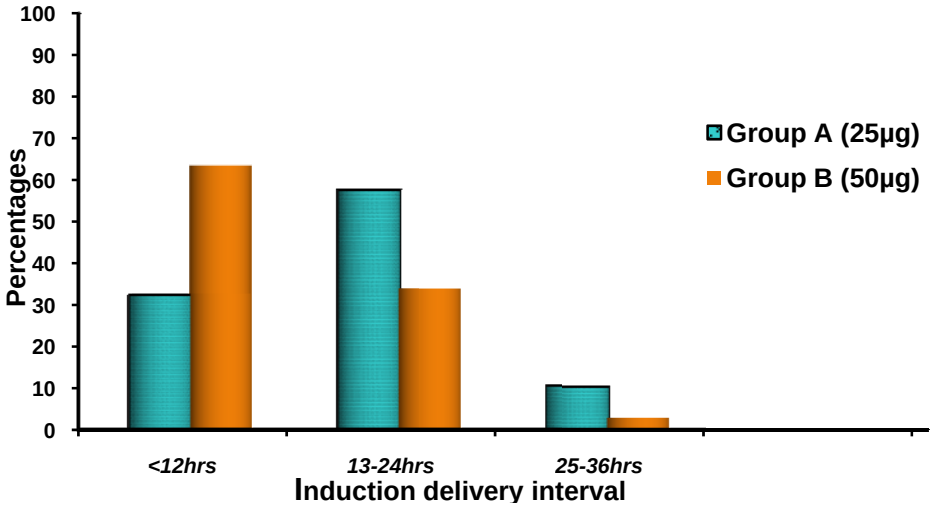
Table 9: Induction delivery interval in vaginally delivered cases

Induction delivery interval (hours)	Group A (25µg) (n=87)		Group B (50µg) (n=71)	
	No	%	No	%
≤12	28	32.2	45	63.4
13-24	50	57.5	24	33.8
25-36	9	10.3	2	2.8
Mean ± SD	16.07±6.71		12.98±4.71	
Inference	Mean Induction delivery interval is significantly less in Group B when compared to Group A with P=0.001**			

** Strongly significant

45 cases (63.4%) delivered within 12 hours of induction in group B (50µg) when compared to only 28 cases (32.2%) in groupA (25µg), with p value of 0.022 which is statistically significant.

Mean induction delivery interval was significantly less in Group B (12.98±4.71) when compared to Group A (16.07±6.71) with P=0.001*



Graph 8: Induction delivery interval

Table 10: Requirement of oxytocin augmentation

Oxytocin augmentation	Group A (25µg) (n=87)		Group B (50µg) (n=71)	
	No	%	No	%
Required	61	70.1	25	35.2
Not required	26	29.9	46	64.8
Inference	Requirement of Oxytocin augmentation is significantly more in Group A with P<0.001**			

**Strongly significant

In groupA (25µg), 61 cases (70.1%) required oxytocin augmentation whereas only 25 cases (35.2%) required oxytocin augmentation in group B (50µg). Thus, the requirement of oxytocin augmentation was significantly more in Group A (25µg) with P<0.001**

Table 11: Mode of delivery

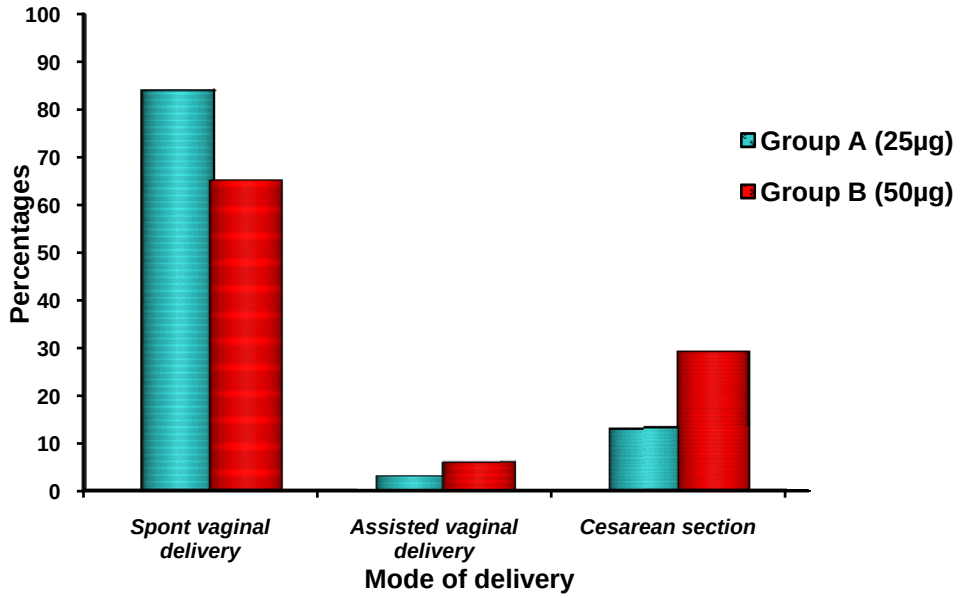
Mode of delivery	Group A (25µg) (n=100)		Group B (50µg) (n=100)	
	No	%	No	%
Spontaneous vaginal delivery	84	84.0	65	65.0
Assisted vaginal delivery	3	3.0	6	6.0
Cesarean section	13	13.0	29	29.0
Inference	LSCS is significantly more associated with Group B (29.0%) when compared to Group A(13.0%) with P<0.001**			

** strongly significant

In group A (25µg) 87% delivered vaginally whereas in group B (50µg) 71% delivered vaginally.

Assisted vaginal delivery was 3% in group A and 6% in group B.

The cesarean section rate was high in group B (29%) when compared to group A (13%) with p<0.001** which was statistically significant.



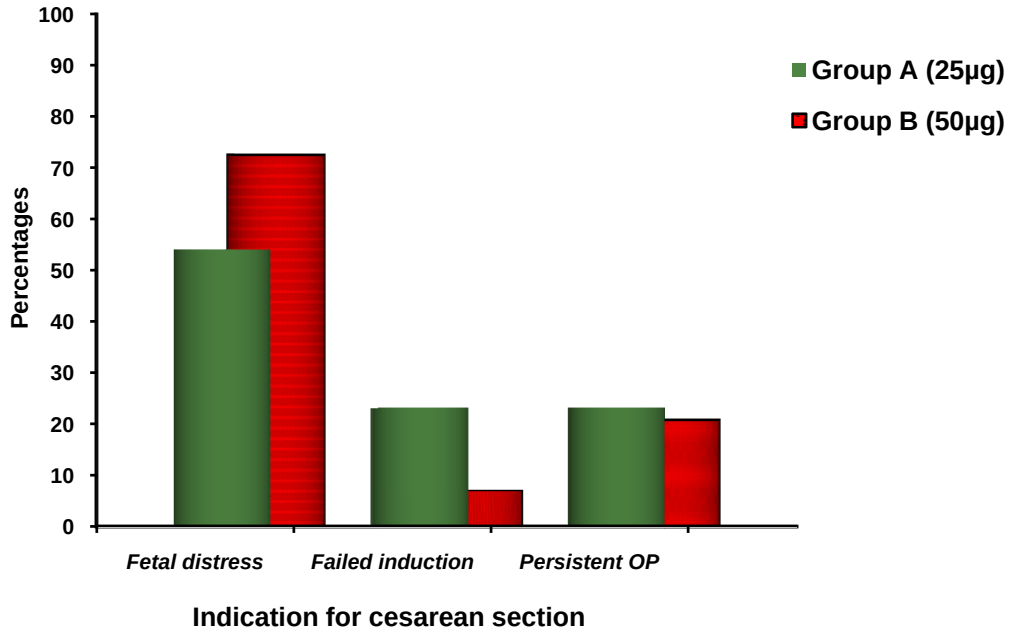
Graph 9: Mode of delivery

Table 12: Indications for cesarean section

Indications for cesarean section	Group A (25µg) (n=13)		Group B (50µg) (n=29)		P value
	No	%	No	%	
Fetal distress	7	53.84	21	72.4	0.238
Failed induction	3	23.0	2	6.8	0.134
Persistent Occipito-posterior presentation	3	23.07	6	20.7	0.862

It was observed that 7/13 (53.84%) in group A (25µg) underwent cesarean section for fetal distress as compared to 21/29 (72.4%) in group B (50µg), but it did not reach statistical significance(p=0.238).

Failed induction was 23% (3/13) in group A when compared to 6.8% (2/29) in group B with p value of 0.134.



Graph 10: Indications for cesarean section

Table 13: Maternal Adverse effects

Maternal Adverse effects	Group A (25µg) (n=100)		Group B (50µg) (n=100)	
	No	%	No	%
Nausea & vomiting	5	5.0	8	8.0
Diarrhea	1	1.0	5	5.0
Fever	2	2.0	6	6.0
Uterine tachysystole	1	1.0	2	2.0
Uterine hypertonus	0	0.0	2	2.0
Uterine hyperstimulation	0	0.0	4	4.0
Postpartum hemorrhage	2	2.0	3	3.0
Total	11	11.0	30	30.0
Inference	Maternal adverse effects are significantly more in Group B (30.0%) when compared to Group A (11.0%) with P=0.001**			

** Strongly significant

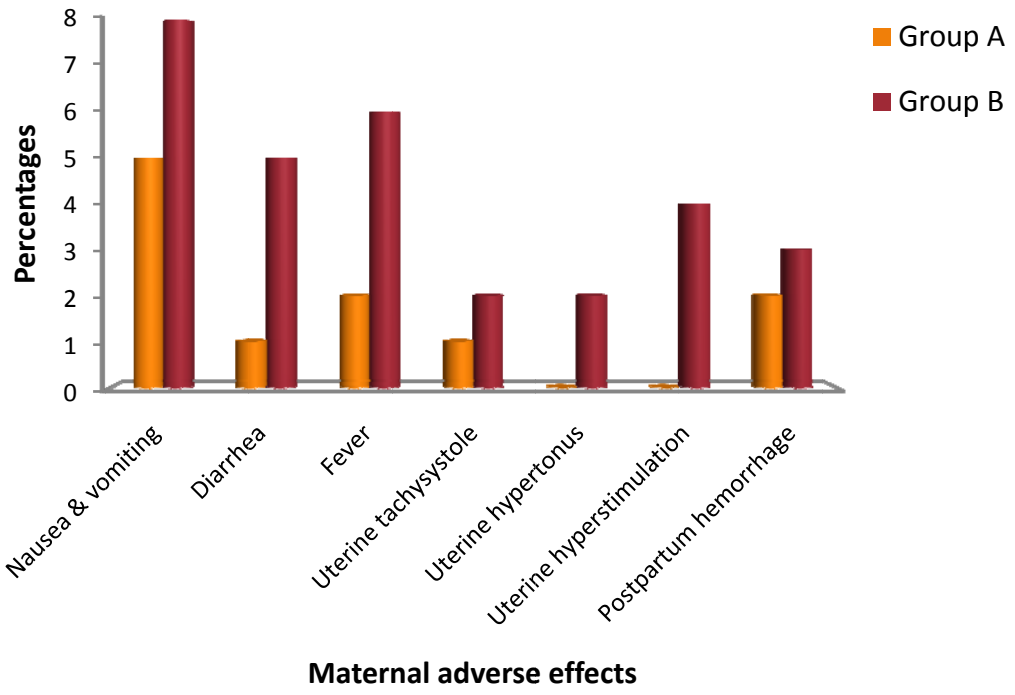
The above table shows the maternal adverse effects between two groups.

Maternal adverse effects are significantly more in Group B (30.0%) when compared to Group A (11.0%) with P=0.001**.

Maternal minor adverse effects (nausea, vomiting, diarrhea and fever) were significantly more in (19 cases) 50µg group when compared to (8 cases) 25µg but did not reach statistical significance (p=0.596).

Abnormal uterine contractions were also more commonly seen in 50µg group (8 cases) than with 25µg group (1 case) but did not reach statistical significance (p=0.385).

Postpartum hemorrhage was almost similar in both the groups i.e. 2% and 3% among group A and B respectively.



Graph 11: Maternal adverse effects

Table 14: Fetal outcome

Fetal outcome	Group A (25µg) (n=100)		Group B (50µg) (n=100)		P value
	No	%	No	%	
Birth weight (kgs)					
<2.5	5	5.0	6	6.0	0.756
2.5-3.5	95	95.0	94	94.0	
>3.5	-	-	-	-	
FHR abnormalities	16	16.0	31	31.0	0.021*
Meconium stained Liquor	18	18.0	32	32.0	0.022*
1 minute Apgar score <7	6	6.0	20	20.0	0.003**
Neonatal resuscitation	18	18.0	32	32.0	0.022*
NICU admission required	5	5.0	15	15.0	0.018*

* Moderately significant

** Strongly significant

The birth weight in both the groups were statistically similar (p=0.756).

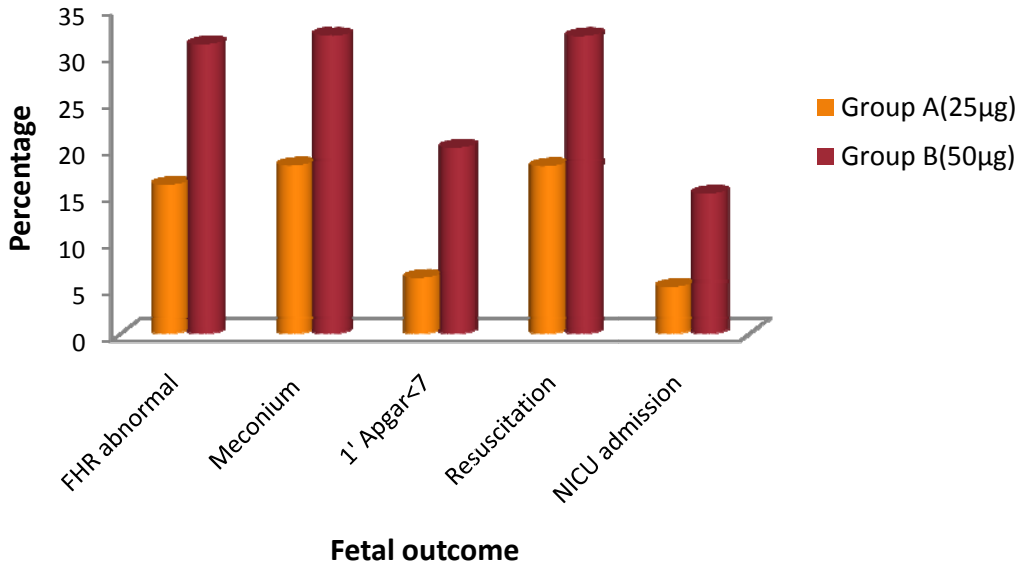
The fetal heart rate abnormalities were significantly high in 50µg group (31%) as compared to25µg group (16%) with p=0.021*.

Meconium stained liquor was more common in group B (32%) than in group A (18%) with p value of 0.022*.

1 minute Apgar score <7 was 20% in group B when compared to only 6% in group A which was statistically significant with p=0.003**.

Neonatal resuscitation was required more in group B (32%) than in group A (18%) with p value of 0.022*.

NICU admission was 15% in group B where as 5% in group A which was statistically significant with p=0.018*.



Graph 12: Fetal outcome

DISCUSSION

Misoprostol the PGE1 analogue appears to be safe and effective but the optimal dose needs to be determined so that successful vaginal deliveries can be accomplished with less number of side effects to the mother and fetus in a short span of time.

This study compares the efficacy and safety of two regimens of vaginal misoprostol for induction of labor and to compare the maternal and fetal outcome.

In the present study the maternal age, parity and gestational age were similar in both the groups.

Indications for induction of labor were statistically similar between both the groups with post-dated pregnancy and pre-eclampsia being the most frequent indications.

According to the study by Farah et al, the most frequent indications for labor induction were pregnancy induced hypertension and premature rupture of membrane.[19]

The mean pre-induction modified bishop score were 3.81±0.84 and 3.62±0.88 in group A (25µg) and group B (50µg) respectively which was statistically similar with p=1.000.

In the present study, mean number of doses received were significantly less in 50µg group when compared to 25µg group (1.76±0.77 vs. 2.13±1.01, p=0.013). Even Meydanli et al (2003) in his study found that the mean number of misoprostol doses was significantly lower in the 50µg group (1.1±0.3 vs. 2.8±0.7, p<0.001).[21]

In the present study, 40.8% in group B (50µg) delivered vaginally after one dose when compared to only 28.7% in group A (25µg) with p value of 0.110 which was statistically not significant.

This was in contrast to the study by Farah et al (1997)which states that 38.2% of patients in 50µg group delivered vaginally after one dose versus 25% of patients in 25µg group ($p < 0.007$).[19]

The study by El-Sherbiny (2001) also support the finding that significantly more women delivered after single dose in 50µg group (53.26%) when compared to 25µg group (27.96%) with $p<0.001$.[20]

Meydanli et al in his study (2003) reported that the proportion of women delivering vaginally with one dose of vaginal misoprostol was significantly greater in the 50µg group ($p < 0.001$)[21]

Various studies	**Vaginal delivery with one dose of misoprostol**		
	25µg Misoprostol	**50µg Misoprostol**	**P value**
Farah et al (1997)[19]	25%	38.2%	<0.007
El-Sherbiny et al (2001)[20]	27.96%	53.26%	<0.001
Meydanli et al (2003)[21]	-	87.23%	<0.001
Present study	28.7%	40.8%	0.110

In the present study, 39.4% (28/71) in group B went into active stage of labor within 6 hours of induction whereas in group A only 27.6% (24/87).

The mean induction to active stage interval was significantly less in Group B (8.32±4.27hrs) when compared to Group A (10.78±5.97 hrs) with P=0.004**

In the present series, 63.4% of patients delivered vaginally within 12 hours of induction in 50µg group when compared to only 32.2% among 25µg group with p=0.022.

This is similar to the study by Meydanli et al (2003). He found that women in 50µg group were more likely to deliver vaginally within 12 hours of labor induction with

vaginal misoprostol when compared with the 25µg group (78.72% vs. 44.89%, p=0.001).[21]

El- Sherbiny et al (2001) in their study said that 70.67% delivered within 12 hours among 50µg group when compared to 46.24% among 25µg group with p<0.05.[20]

Gupta et al (2010) in his study observed that 43.9% delivered within 12 hours among 50µg group when compared to only 29.1% among 25µg group.[43]

In contrast, Farah et al (1997) in his study found no difference among the two groups with regard to delivery within 12 hours of induction (75.5% vs 72.9%).[19]

Various studies	% of cases delivered vaginally within 12 hours		
	25µg Misoprostol	50µg Misoprostol	P value
Farah et al (1997)[19]	75.5%	72.9%	Not significant
El-Sherbiny et al (2001)[20]	46.24%	70.67%	< 0.05
Meydanli et al (2003)[21]	44.89%	78.72%	0.001
Gupta et al (2010)[43]	29.1%	43.9%	Not mentioned
Present study	32.2%	63.4%	0.022

In the present study, the mean induction delivery interval was significantly shorter (12.98±4.71 hours) in 50µg group when compared to (16.07±6.71 hours) 25µg group with p= 0.001**.

This was comparable to study by El-Sherbiny et al (2001) which reported that induction delivery interval was shorter in 50µg group when compared to 25µg group (17.18±8.48 hrs vs.9.37±5.87 hrs, p<0.05). Similar result was reported by Elhassan et al (2005), the mean induction delivery interval was significantly longer in the 25µg when compared to 50µg group (21.9±4.3h vs 9.6±2.2h, p=0.04).[24]

Farah et al (1997) in their study found that induction delivery interval was almost similar in two groups (895±572 min vs. 787±538 min, p value not significant).[19]

Meydanli et al (2003) in his study also found no difference in the induction delivery interval among two groups (685±201 min vs 627±177 min, p=0.09).[21]

Various studies	Mean induction-delivery interval		
	25µg Misoprostol	**50µg Misoprostol**	**P value**
Farah et al (1997)[19]	895±572 minutes	787±538 minutes	Not significant
El-Sherbiny et al (2001)[20]	17.18±8.48 hours	9.37±5.87 hours	< 0.05
Meydanli et al (2003)[21]	685±201 minutes	627±177 minutes	0.09
Elhassan et al (2005)[24]	21.9±4.3 hours	9.6±2.2 hours	0.04
Present study	16.07±6.71 hours	12.98±4.71 hours	0.001

In the present study, the oxytocin augmentation was required less in 50µg group when compared to 25µg group (70.1% vs. 35.2%, p<0.001**) which is comparable to the study done by Gupta et al and Farah et al.[19, 43]

A Cochrane review by Hofmeyer (2010) also revealed that lower doses were associated with more need for oxytocin augmentation.[25]

In the present study, 87% delivered vaginally in group A (25µg) and 71% delivered vaginally in group B (50µg). Cesarean section was more common among 50µg group, 29% when compared to 13% in 25µg group. This was statistically significant with p value of < 0.001.

In contrast, Elhassan et al (2005) in his study reported that cesarean section rate was significantly high in the 25µg group (32.3% vs 6.3%, p=0.05).[24]

Meydanli et al (2003) in his study said that there was no significant difference in the rate of cesarean section in the two treatment groups (18.3% vs. 21.6% p=0.6).[21]

There was no statistically significant difference in the incidence of operative vaginal delivery between the two groups (3% vs 6%) comparable to the study by Meydanli et al.[21]

In a recent review comparing 25µg vs. 50µg of intravaginal misoprostol for labor induction, Sanchez-Ramos et al also reported that no dose related difference were noted with regard to the rates of cesarean and operative vaginal deliveries.[44]

Various studies	Mode of delivery		
	25µg Misoprostol	**50µg Misoprostol**	**P value**
Farah et al (1997)[19]			
Vaginal delivery	88%	84.1%	Not significant
Operative vaginal delivery	Not mentioned	Not mentioned	Not mentioned
Cesarean section	12%	15.9%	Not significant
Meydanli et al (2003)[21]			
Vaginal delivery	81.6%	78.3%	0.6
Operative vaginal delivery	3.3%	5%	0.6
Cesarean section	18.3%	21.6%	0.6
Elhassanet al (2005)[24]			
Vaginal delivery	61.3%	90.6%	0.02
Operative vaginal delivery	6.5%	3.1%	0.15
Cesarean section	32.3%	6.3%	0.05
Present study			
Vaginal delivery	87%	71%	
Operative vaginal delivery	3%	6%	
Cesarean section	13%	29%	<0.001

In the present study, 53.84% underwent cesarean section for fetal distress among 25µg group when compared to 72.4% among 50µg group with p=0.238.

This was comparable to study by Hans et al (2002). In his study the rate of cesarean section due to fetal distress was higher with the 50µg doses (28.6% vs 10.3%, p< 0.05).[45]

Gupta et al (2010) in his study also reported that the rate of cesarean section due to fetal distress was higher with 50µg (40% vs 81.81%). [43]

Farah et al (1997) in his study did not find any significance among the two groups with regard to cesarean section for fetal distress (30.4% vs. 48.5%, p value not significant).[19]

Meydanli et al (2003) also did not find any difference among two groups in cesarean section rate for fetal distress (13.3% vs. 15%, p=0.9).[21]

Various studies	**Rate of cesarean section for fetal distress**		
	25µg Misoprostol	**50µg Misoprostol**	**P value**
Farah et al (1997) [19]	30.4%	48.5%	Not significant
Hans et al (2002) [45]	10.3%	28.6%	<0.05
Meydanli et al (2003) [21]	13.3%	15%	0.9
Gupta et al (2010) [43]	40%	81.81%	Not mentioned
Present study	53.84%	72.4%	0.238

The cases with failed induction were more common with 25µg (23%) as compared to those in 50µg group (6.8%) though it did not reach statistical significance (p=0.134). This finding was consistent with the study of Meydanli et al and Gupta et al.[21,43]

Maternal adverse effects were more common among 50µg group (30%) when compared to 25µg group (11%), p=0.001, but catastrophic side effects like uterine rupture did not occur in any of the cases in our study. This was comparable to the study by Gupta et al.[43]

Maternal minor adverse effects (nausea, vomiting, diarrhea and fever) were significantly more in 50µg group (19 cases) when compared to 25µg group (8 cases) but did not reach statistical significance (p=0.596).

Abnormal uterine contractions were more common with 50µg of misoprostol (8 cases) than with 25µg (1 case) but did not reach statistical significance (p=0.385) and the incidence of postpartum hemorrhage were comparable in both the groups (2% vs 3%).

However, El-Sherbiny et al in their study reported that tachysystole was significantly more common with 50µg. Atonic PPH was also found to be more common with 50µg group(9.78% vs. 2.15%, p<0.05).[20]

In the present study, meconium stained liquor was seen in 32% of cases among 50µg group compared to 18% among 25µg group which was statistically significant (p=0.022). This was contrast to the study by Meydanli et al and Elhassan et al, where there was no significant difference between two groups in meconium stained amniotic fluid.[21, 24]

Various studies	**Meconium stained liquor**		
	25µg Misoprostol	**50µg Misoprostol**	**P value**
Meydanli et al (2003)[21]	15%	10%	0.4
Elhassan et al (2005)[24]	6.5%	9.3%	0.65
Present study	18%	32%	0.022

In our study neonatal outcome was also adversely affected in cases who received 50µg of misoprostol. The fetal heart rate abnormalities was 31% in 50µg group as compared to 16% in 25µg group with p=0.021*.

1 minute Apgar score <7 was 20% in group B when compared to only 6% in group A which was statistically significant with p=0.003**.

Neonatal resuscitation was required more in group B (32%) than in group A (18%) with p value of 0.022*. NICU admission was 15% in group B when compared to 5%

in group A which was statistically significant with p=0.018*, this was in concurrence with the observation made by Gupta et al.[43]

Contrary to this, Farah et al (1997) reported comparable neonatal outcomes with the two doses. [45]

Various studies	Fetal outcome		
	25µg Misoprostol	**50µg Misoprostol**	**P value**
Farah et al (1997)[19]			
1' Apgar score<7	17.2%	18.8%	Not significant
NICU admission	5.7%	11.1%	Not significant
Gupta et al (2010) [43]			
1' Apgar score<7	14.9%	34.7%	Not mentioned
NICU admission	16.4%	35.6%	Not mentioned
Present study			
1' Apgar score<7	6%	20%	0.003
NICU admission	5%	15%	0.018

CONCLUSION

Misoprostol as a method of induction of labor intravaginally in dosage of 50µg is more efficacious than 25µg in terms of shorter induction delivery interval and less oxytocin augmentation, but it is less safe both for the mother and the fetus due to high cesarean section rate, high incidence of abnormal uterine contractions, FHR abnormalities, meconium stained liquor, low Apgar score and NICU admission.

SUMMARY

1.In the present study the maternal age, parity and gestational age were similar among both the groups.

2. The mean pre-induction modified bishop score in group A(25µg) was 3.81±0.84 and in group B (50µg) was 3.62±0.88 with p value of 1.000, which was statistically similar in two groups.

3. Indications for induction were statistically similar between both the groups with post-dated pregnancy and pre-eclampsia/eclampsia being the most frequent indications for labor induction.

4. Mean number of doses required was significantly less in 50µg group when compared to 25µg group (1.76±0.77 vs. 2.13±1.01, p=0.013).

5. 40.8% in group B (50µg) delivered vaginally with single dose when compared to only 28.7% in group A (25µg) with p value of 0.110 which was statistically not significant.

6. The mean induction to active stage interval was significantly shorter among group B (8.32 hrs) when compared to group A (10.78 hrs) with p=0.004**

7. 63.4% of patients delivered vaginally within 12 hours in 50µg group when compared to only 32.2% among 25µg group with p=0.022**.**

8.The mean induction delivery interval was significantly less (12.98±4.71 hours) in 50µg group when compared to (16.07±6.71 hours) 25µg group with p= 0.001.

9. Oxytocin augmentation was required less in 50µg group when compared to 25µg group (70.1% vs. 35.2%, p<0.001**)

10.In group A (25µg) 87% delivered vaginally and in group B (50µg) 71% delivered vaginally. Cesarean section was more common among 50µg group (29%) when

compared to (13%) 25µg group. This was statistically significant with p value of < 0.001.

11. There was no statistically significant difference in the incidence of operative vaginal delivery between the two groups (3% vs 6%).

12. In present study, 53.84% underwent cesarean section for fetal distress among 25µg group when compared to 72.4% in50µg group with p=0.238.

13. The cases with failed induction were more common with 25µg (23%) as compared to those in 50µg group (6.8%) though it did not reach statistical significance (p=0.134).

14. Maternal adverse effects were more common in 50µg group (30%) when compared to 25µg group (11%), p=0.001.

15. Abnormal uterine contractions were more common with 50µg of misoprostol than with 25µg but did not reach statistical significance (p=0.385).

16. Postpartum hemorrhage was similar in both the groups i.e. 2% and 3% among group A and B respectively.

17.The fetal heart rate abnormalities were significantly high in 50µg group (31%) as compared to25µg group (16%) with p=0.021.

18. Meconium stained liquor was more common in group B (32%) than in group A (18%) with p value of 0.022.

19. 1 minute Apgar score <7 was 20% in group B (50µg) when compared to only 6% in group A (25µg)which was statistically significant with p=0.003.

20. Neonatal resuscitation was required more in group B (32%) than in group A (18%) with p value of 0.022.

21. NICU admission was 15% in group B (50µg) where as 5% in group A (25µg) which was statistically significant with p=0.018.

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PROFORMA

Name :

Age:

Occupation :

Address:

IP NO:

DOA:

DOD:

Diagnosis :

H/O presenting complaints:

Obstetric history: Married life:

Consanguineous/Non consanguineous:

Gravida :

Para:

Abortions:

Living/Dead:

Previous pregnancy details

Present pregnancy details :

Menstrual history: Age of menarche:

Previous menstrual cycles :

LMP : EDD : POG :

Past history:

Family history:

Personal history: Diet:

Appetite:

Sleep:

Bowel/Bladder habits:

Addiction:

General physical examination :

Built:

Nourishment:

Height:

Weight:

BMI:

Pallor Icterus Clubbing Cyanosis Lymphadenopathy Edema

Breast /spine/thyroid:

Vital signs:

Pulse

BP:

Temp:

Systemic examination:

CVS/RS:

Per abdomen: Uterus size:

Relaxed /Acting :

Presentation:

FHS:

Per vagina:

Modified Bishop score:

Favourable / Unfavourable:

Pelvis adequate/ inadequate:

CTG:

DETAILS OF DELIVERY:

Time of initiation of induction:

Time interval between each induction:

Total dose of induction:

Induction delivery interval:

a) Induction to active stage:

b) Active stage to delivery

Use of oxytocin for augmentation:

Vaginal delivery / Cesarean section:

Failed induction: Yes /No

Indication for cesarean section

Maternal abnormal uterine contractions:

DETAILS OF NEONATE:

Sex:

Birth weight:

APGAR:

Requirement of resuscitation:

Admission to NICU:

INVESTIGATIONS:

Hemoglobin:

PCV:

Blood group:

RBS:

HIV/HbsAg/VDRL:

Urine analysis:

Obstetric ultrasound:

KEY TO MASTER CHART

IP.No: In Patient number

POG: Period of gestation in weeks

IFI: Indication for induction

A: Postdated pregnancy

B: Post-term pregnancy

C: Oligohydramnios

D: IUGR

E: Isoimmunisation

F: GDM

G:Pre-eclampsia

H: Eclampsia

PIMBS: Pre-induction Modified Bishop Score

NOD: Number of doses

IAS: Induction to active stage interval in hours

IDI: Induction delivery interval in hours

MOD: Mode of delivery

V- Vaginal

I- Instrumental

C- Cesarean section

IFC: Indication for cesarean section

FD- Fetal distress

FI- Failed induction

POPP- Persistent Occipito-posterior presentation

OA: Oxytocin augmentation

R- Required

NR- Not required

Baby details- Sex (M-Male, F-Female) and weight in kgs

MSL: Meconium Stained Liquor - Yes/No

1'Apgar score:>7 – A,<7 – B

NICU Admission:

Yes- Required

No – not required

MatAddEff: Maternal Adverse effects

A: Nausea, vomiting

B: Diarrhea

C: Fever

D: Uterine tachysystole

E: Uterine hypertonus

F: Uterine hyperstimulation

G: Postpartum hemorrhage

Sl No	Hosp.No	Age	Group	gravida	POG	IFI	PIMBS	NOD	IAS	IDI	MOD	IFC	OA	BabyDetail	MSL	APGAR	NICUadm	MatAdvEff
1	693404	27	A	P	40+6	A	4	2	12	18	V		R	F,3kg	No	A	No	
2	659858	30	B	P	37+6	G	2	…..		….	C	FD	…	M,2.7kg	No	A	No	A
3	693433	30	A	M	39+1	G	3	1	5	8	V		NR	M,2.6kg	No	A	No	
4	660105	24	B	P	37+0	H	4	1	5	10	I		NR	M,3kg	No	A	No	G
5	694401	30	A	M	41+2	A	3	…..		….	C	FD	….	M,3kg	Yes	B	Yes	
6	660045	22	B	P	40+5	A	3	3	16	23hr30min	V		R	M,2.9kg	No	A	No	A
7	696697	21	A	P	39+1	G	5	2	8	14	V		NR	F,2.8kg	No	A	No	
8	625176	27	B	M	40+2	A	4	2	9	12	V		R	F,3.3kg	No	A	No	
9	702266	20	A	P	40+5	A	4	2	9	13	V		R	F,2.5kg	No	A	No	
10	647722	28	B	P	41+1	A	5	1	3	6	V		NR	M,3.5kg	No	A	No	
11	695976	23	A	M	39+5	G	3	2	8	12	V		R	F,3kg	No	A	No	
12	694896	22	B	M	39+0	A	3	2	8	12hr45mn	I		NR	M,3.5kg	No	A	No	B
13	700974	22	A	P	41+4	A	3	1	3	7	V		NR	M,3.2kg	No	A	No	
14	691580	21	B	M	42+1	B	4	1	5	10	V		NR	F,2.5kg	No	A	No	
15	704192	25	A	P	39+0	G	3	5	29	36	V		R	F,2.5kg	Yes	B	Yes	C
16	704091	25	B	M	39+1	G	2	3	16	22	V		NR	M,3.4kg	Yes	B	Yes	A
17	705763	28	A	M	41+4	A	4	1	5	8	V		R	F,2.5kg	No	A	No	
18	700172	22	B	P	41+1	A	2	2	9	15	V		NR	M,3kg	No	A	No	
19	712564	25	A	M	40+1	G	2	….		…	C	POPP	….	M,2.8kg	Yes	A	No	
20	705485	24	B	M	40+1	E	3	1	6	12	V		NR	M,2.5kg	No	A	No	
21	712787	22	A	P	42+3	B	3	5	28	34	V		R	M,2.8kg	No	A	No	A
22	701523	19	B	M	40+1	G	5	2	9	12	V		NR	F,3kg	No	A	No	
23	715928	25	A	P	39+2	G	3	3	18	24	V		R	M,3.15kg	No	A	No	
24	701156	30	B	P	40+1	E	5	1	3	6	V		R	F,2.8kg	No	A	No	
25	771482	26	A	M	40+4	A	4	2	10	15	V		R	M,3.4kg	No	A	No	
26	711920	25	B	M	42+1	B	4	2	8	12	V		NR	M,2.5kg	No	A	No	
27	669544	23	A	M	41+3	A	3	2	10	15	V		R	F,3kg	No	A	No	
28	711753	18	B	P	38+1	G	3	2	9	14	V		NR	M,2.5kg	No	A	No	A
29	692280	24	A	P	40+2	G	3	….		….	C	FD	…	F,2.8kg	Yes	B	No	
30	600180	25	B	M	40+2	C	2	2	10	18	V		R	M,3kg	No	A	No	C
31	716307	20	A	P	42+6	B	4	3	16	20	V		R	F,2.7kg	No	A	No	
32	752152	28	B	P	40+3	G	3	2	10	15	V		R	M,3kg	No	A	No	D,F
33	719453	28	A	M	40+2	A	3	…		….	C	FD	R	F,3.37kg	Yes	B	Yes	

34	663318	26	B	M	40+1	G	5	1	3	8	V		NR	F,3kg	No	A	No	
35	720583	23	A	P	40+6	A	4	2	10	16	V		R	F,2.5kg	No	A	No	
36	656636	23	B	M	41+4	A	4	1	6	11	V		NR	F,2.9kg	No	A	No	
37	677392	23	A	P	41+1	A	5	1	4	7	V		NR	F,3.2kg	No	A	No	
38	720169	19	B	P	39+6	G	2	….		….	C	POPP	…	M,3.2kg	No	A	No	
39	720835	23	A	M	40+4	A	4	1	4	7	V		R	F,3kg	No	A	No	
40	719681	19	B	M	40+1	D	3	2	9	12	V		NR	F,2.5kg	No	A	No	G
41	722173	24	A	P	41+1	A	5	1	3	6	V		NR	F,3.2kg	No	A	No	
42	721558	19	B	P	39+2	C	3	….		…..	C	FD	….	M,3.2kg	Yes	B	Yes	A
43	752152	26	A	M	38+1	G	2	3	15	20	V		R	M,2.8kg	Yes	A	No	
44	624355	24	B	M	40+1	C	4	1	3	6	V		NR	F,3kg	No	A	No	
45	740581	25	A	P	41+1	A	4	2	9	13	V		R	M,3.4kg	No	A	No	
46	741279	24	B	M	38+6	G	4	….		…	C	FD	…	M,2.5kg	Yes	B	Yes	
47	717861	23	A	P	40+1	E	5	….		….	C	FD	…	F,3kg	No	A	No	
48	742474	20	B	P	40+3	A	3	2	9	12	V		NR	F,3.3kg	No	A	No	B
49	726075	27	A	M	39+2	G	3	4	24	30	V		R	M,3.5kg	Yes	A	No	
50	751393	25	B	M	40+1	G	3	2	9	12	V		NR	F,2.8kg	No	A	No	
51	742480	20	A	P	38+1	G	4	2	11	17	V		R	F,2.4kg	No	A	No	
52	742878	18	B	M	39+2	G	2	…..		…	C	FI	….	F,2.5kg	No	A	No	A,C
53	775123	24	A	P	41+2	A	4	3	15	20	V		R	M,2.8kg	No	A	No	B
54	742836	19	B	P	40+6	A	4	2	12	17	V		NR	M,3kg	No	A	No	
55	744893	35	A	M	42+1	B	2	…..		…	C	FI	…	M,3.3kg	No	A	No	G
56	739524	22	B	M	40+0	F	3	….		….	C	FI	…	M,2.9kg	No	A	Yes	A
57	744198	20	A	P	40+6	A	3	1	5	8	V		NR	F,3kg	No	A	No	
58	744468	18	B	M	41+3	A	3	1	6	11	V		R	M,2.75kg	No	A	No	
59	746170	24	A	M	42+1	B	5	**…**		….	C	FD	…	F,2.4kg	Yes	A	No	
60	746366	24	B	P	40+1	G	3	2	12	18hr30min	V		R	F,2.5kg	Yes	B	Yes	C
61	745545	20	A	P	37+6	G	4	2	9	12	V		R	F,2.4kg	No	A	No	
62	746876	22	B	P	38+3	G	3	…		…..	C	DTA	…	F,2.5kg	Yes	B	Yes	
63	748158	20	A	P	41+3	A	5	1	5	8	V		NR	F,3kg	No	A	No	
64	749404	24	B	M	37+2	G	4	….		…	C	FD	….	F,2.6kg	No	A	No	
65	753457	25	A	P	40+6	A	4	1	5	8	V		NR	F,3.25kg	No	A	No	
66	750846	24	B	M	41+1	A	3	2	12	18	V		R	F,3kg	No	A	No	
67	751755	22	A	M	39+2	G	3	3	18	26	V		R	M,2.8kg	No	A	No	

68	754481	24	B	P	41+6	A	5	1	6	11	V		NR	M,2.9kg	No	A	No	
69	664032	20	A	M	40+0	G	3	4	20	26	V		R	M,2.6kg	No	A	No	
70	748093	23	B	P	38+3	G	3	3	14	18	V		R	M,3kg	No	A	No	
71	752448	25	A	P	41+3	A	4	2	12	18	V		R	M,3.5kg	No	A	No	
72	752748	26	B	M	42+1	B	3	…		…	C	FD	…	F,3.2kg	Yes	B	Yes	
73	754692	22	A	M	39+3	G	3	2	8	13	V		R	F,3kg	No	A	No	
74	752814	22	B	P	40+0	G	4	3	15	20	V		R	M,3kg	Yes	A	No	
75	723847	27	A	M	41+4	A	4	1	8	12	V		R	F,3.25kg	Yes	A	Yes	
76	702984	28	B	P	42+3	B	5	1	4	9	V		NR	F,2.75kg	No	A	No	
77	757416	26	A	P	40+3	G	3	2	11	16	V		NR	F,3.24kg	No	A	No	
78	758472	21	B	M	38+1	H	4	2	9	12	V		R	F,2.25kg	No	A	No	
79	758439	22	A	M	40+6	A	3	2	11	16	V		NR	F,2.75kg	No	A	No	
80	694416	22	B	P	41+1	A	5	……		…..	C	DTA	…..	F,3kg	No	A	No	
81	714521	30	A	P	42+1	B	5	1	4	7	V		NR	M,2.5kg	No	A	No	
82	695300	21	B	P	40+4	A	3	2	9	12	V		R	F,2.37kg	Yes	B	Yes	D,F
83	753392	29	A	M	41+3	A	3	3	15	21	V		R	M,2.9kg	No	A	No	
84	741482	30	B	M	37+5	G	4	2	9	12	V		R	F,2.5kg	No	A	No	
85	759720	27	A	P	38+5	G	5	1	4	10	V		NR	F,2.5kg	No	A	No	
86	746390	24	B	M	41+4	A	3	….		…	C	POPP	…..	M,3.5kg	Yes	B	Yes	G*
87	756285	22	A	P	40+6	A	5	2	10	16	V		R	F,2.6kg	No	A	No	
88	761445	28	B	P	39+5	G	4	….		….	C	FD	….	M,3.5kg	Yes	B	Yes	
89	753331	29	A	M	41+1	A	3	5	28	36	I		R	M,2.9kg	Yes	A	No	A
90	753392	24	B	M	40+2	G	3	3	16	22	V		R	M,3kg	No	A	No	
91	762290	30	A	M	41+4	A	5	1	4	9	V		NR	F,2.9kg	No	A	No	
92	762436	20	B	P	40+1	A	5	2	9	13	V		R	F,2.37kg	No	A	No	
93	751125	30	A	M	40+4	G	5	1	4	9	V		NR	M,2.7kg	No	A	No	
94	763679	19	B	M	40+6	A	3	…		….	C	FD	….	M,2.7kg	Yes	B	Yes	C
95	751125	20	A	P	40+5	A	4	2	11	16	V		R	F,3kg	No	A	No	
96	757577	24	B	M	40+1	C	5	1	3	7	V		NR	F,2.75kg	No	A	No	
97	752151	26	A	P	40+6	A	3	2	10	16	V		R	F,2.75kg	No	A	No	
98	762231	26	B	M	40+3	G	2	…		…	C	FD	…..	F,3kg	Yes	A	No	
99	778152	20	A	P	40+0	G	4	3	15	21	V		R	M,2.9kg	No	A	No	
100	781521	25	B	M	39+6	G	4	1	6	11	V		NR	F,3kg	No	A	No	
101	785162	22	A	P	39+2	G	2	….		…	C	FD	….	M,3.15kg	Yes	B	No	A,C

102	774485	26	B	M	39+3	G	5	2	9	13	V		NR	F,3kg	No	A	No	
103	776322	24	A	P	42+1	B	4	3	15	20	V		R	M,3.2kg	No	A	No	
104	765544	29	B	M	40+2	C	3	2	9	12	V		NR	M,2.8kg	No	A	No	A
105	765554	29	A	M	41+1	A	4	3	16	21	V		R	F,3kg	No	A	No	
106	756454	26	B	P	40+4	A	3	….		….	C	FD	…..	M,3.15kg	Yes	B	No	
107	786778	25	A	P	39+2	G	4	2	10	15	I		R	F,2.8kg	No	A	No	
108	754676	23	B	M	41+0	A	3	1	4	9	V		NR	F,2.5kg	No	A	No	
109	756492	22	A	M	41+6	A	3	4	21	26	V		R	F,3kg	No	A	No	A
110	808712	25	B	M	39+1	G	4	1	3	8	V		NR	M,2.6kg	No	A	No	
111	778956	26	A	M	42+2	B	3	3	16	21	V		R	M,2.75kg	No	A	No	
112	798610	30	B	P	41+2	A	3	…		…..	C	FD	…	F,3kg	Yes	B	No	
113	798435	26	A	P	38+4	G	4	2	10	15	V		R	M,2.7kg	No	A	No	
114	786654	24	B	M	39+5	G	5	1	5	10	I		NR	F,3kg	No	A	No	
115	800431	31	A	M	41+0	A	4	2	9	12	V		R	F,2.7kg	Yes	A	No	
116	790789	25	B	P	41+6	A	3	…	…..	…	C	FD	….	M,2.6kg	No	B	No	
117	792789	25	A	P	39+5	C	4	2	11	16	V		R	M,2.7kg	No	A	No	
118	800921	26	B	M	40+6	A	4	1	4	9	V		NR	F,3kg	No	A	No	
119	799912	24	A	M	39+7	G	3	3	15	21	V		R	F,2.6kg	No	A	No	
120	765234	27	B	P	41+2	A	3	2	9	13	I		NR	F,3.1kg	Yes	A	No	
121	745698	24	A	P	41+5	A	3	3	15	21	V		R	F,2.6kg	No	A	No	
122	801120	22	B	M	38+5	G	2	2	9	12	V		NR	M,3.15kg	No	A	No	
123	791019	27	A	M	42+2	B	3	4	21	27	V		R	M,3.12kg	No	A	No	A
124	780012	21	B	P	41+2	A	4	….	…..	…	C	FD	…	F,3kg	Yes	B	No	
125	782310	23	A	P	41+3	A	3	2	10	16	V		R	M,3.1kg	No	A	No	
126	809868	22	B	M	40+6	A	3	….	…..	….	C	DTA	….	M,3.3kg	No	B	No	
127	792211	24	A	M	40+5	A	4	2	10	16	V		NR	F,2.8kg	Yes	A	No	
128	768811	25	B	P	39+6	G	2	….	….	…	C	FD	…..	M,2.8kg	Yes	A	No	
129	801021	26	A	P	41+2	A	3	3	15	21	V		R	M,2.6kg	No	A	No	
130	791598	27	B	P	41+3	G	3	2	9	12	I		R	F,3.1kg	Yes	A	No	B
131	791758	20	A	M	41+4	A	5	1	6	10	V		R	M,2.8kg	No	A	No	
132	777990	23	B	P	38+2	G	4	2	9	12	V		R	F,2.5kg	No	A	No	
133	747977	20	A	P	41+0	A	3	…	…..	….	C	FI	….	F,2.7kg	Yes	A	No	A
134	778925	25	B	P	39+3	G	3	…	…..	….	C	FD	….	M,2.8kg	Yes	B	No	
135	781239	26	A	M	38+4	G	4	…	…..	…	C	POPP	….	F,2.8kg	No	A	No	

136	804373	27	B	M	40+5	A	5	1	4	8	V		NR	F,2.6kg	No	A	No	
137	803701	30	A	M	40+4	A	4	2	10	15	V		R	F,2.9kg	No	A	No	
138	796765	20	B	P	40+1	G	3	2	9hr30min	14	V		NR	F,2.3kg	No	A	No	
139	796730	21	A	P	40+6	A	4	2	12	18	V		R	M,2.8kg	No	A	No	
140	796320	19	B	M	39+6	G	3	…..	…..	…..	C	FD	….	F,2.5kg	Yes	A	No	
141	795125	26	A	M	39+5	C	5	1	6	10	V		R	F,2.9kg	No	A	No	
142	602252	21	B	M	38+2	G	3	2	9	14	V		NR	M,3kg	Yes	A	No	
143	795104	30	A	M	39+0	G	4	2	9	15	V		R	M,3.2kg	No	A	No	
144	775122	32	B	P	40+0	G	5	1	6	11	V		R	M,2.8kg	No	A	No	
145	796390	24	A	M	40+5	A	3	3	15	22	V		R	M,3.2kg	No	A	No	
146	798880	25	B	P	41+4	A	4	1	4	9	V		NR	M,2.8kg	No	A	No	
147	734311	26	A	P	40+1	C	5	…..	…..	…..	C	FI	….	M,2.8kg	No	A	No	
148	802139	20	B	P	37+2	H	3	2	9	12	V		NR	M,2.5kg	No	A	No	
149	748351	25	A	P	42+0	B	3	2	10	16	V		R	M,3.09kg	No	A	No	
150	792844	23	B	P	39+3	G	4	2	9	12	V		NR	F,3kg	No	A	No	
151	800466	24	A	P	38+4	G	4	2	10	16	V		R	M,2.6kg	No	A	No	
152	735084	24	B	M	40+2	C	5	1	7	12	V		NR	F,3kg	No	A	No	
153	800805	25	A	M	41+1	A	4	3	15	24	V		R	M,2.7kg	No	A	No	
154	767871	22	B	P	39+3	G	4	1	6	10	V		NR	M,2.8kg	Yes	A	No	A
155	781514	30	A	M	40+3	G	5	2	10	16	V		NR	F,3kg	Yes	A	No	
156	780442	22	B	M	40+5	A	4	3	15	21	V		NR	F,2.8kg	No	A	No	C
157	800773	28	A	M	39+5	C	4	1	3	8	V		NR	M,3kg	No	A	No	
158	792844	23	B	P	40+2	G	4	2	9	15	V		R	F,3kg	No	A	No	
159	801543	28	A	M	41+2	A	3	4	21	28	V		R	M,2.7kg	No	A	No	D
160	800773	29	B	M	40+1	A	3	3	16	21	V		NR	M,2.9kg	No	A	No	
161	800808	28	A	M	41+1	A	4	3	17	24	I		R	M,2.9kg	No	A	No	
162	795125	26	B	M	39+4	G	3	….	…..	…	C	FD	….	F,3kg	Yes	B	No	
163	796390	24	A	P	40+6	A	5	1	6	11	V		NR	M,3.2kg	No	A	No	
164	798880	25	B	M	41+3	A	4	1	4	9	V		NR	F,2.8kg	No	A	No	
165	805125	26	A	P	40+1	G	5	1	3	9	V		NR	M,3kg	Yes	A	No	
166	801415	26	B	P	39+0	G	3	3	15	21	V		NR	M,2.7kg	Yes	A	No	
167	808663	30	A	M	39+3	G	5	1	3	8	V		NR	F,2.8kg	No	A	No	
168	809321	25	B	P	41+1	A	3	…	…..	….	C	FD	…..	F,2.6kg	Yes	A	No	E,F
169	810827	19	A	M	40+5	A	4	1	3	9	V		R	M,2.6kg	No	A	No	G

170	785435	28	B	M	38+4	F	4	1	4	10	V		NR	F,3.5kg	No	A	Yes	
171	788977	25	A	P	41+3	A	4	2	11	16	V		R	F,3.4kg	No	A	No	
172	799760	24	B	M	40+6	A	4	2	9	13	V		NR	M,2.9kg	No	A	No	B
173	812443	23	A	P	41+6	A	4	2	9	13	V		R	M,2.5kg	No	A	No	
174	811725	26	B	P	39+3	G	2	4	21	26	V		R	F,3.4kg	Yes	A	No	C
175	816738	22	A	M	40+6	A	3	3	16	21	V		R	M,2.7kg	No	A	No	
176	817531	23	B	P	38+6	C	4	2	10	16	I		R	F,2.6kg	Yes	B	Yes	
177	817843	19	A	P	41+6	A	3	….	…..	…	C	DTA	….	M,3.2kg	No	A	No	
178	817823	27	B	M	38+1	G	4	1	3	8	V		NR	M,2.7kg	No	A	No	B
179	818181	24	A	P	41+2	A	4	2	11	18	V		R	M,2.47kg	Yes	A	No	
180	818913	21	B	M	41+1	A	3	….	…..	….	C	FD	….	M,3.3kg	Yes	A	No	
181	821488	20	A	P	38+3	G	4	1	4	11	V		R	F,2.8kg	No	A	No	
182	821811	22	B	P	39+3	G	3	4	21	28	V		NR	M,2kg	No	B	Yes	
183	821303	20	A	M	41+2	A	5	1	3	8	V		R	F,3.2kg	Yes	A	No	
184	773590	25	B	M	41+3	A	4	1	3	9	V		NR	F,2.7kg	No	A	No	
185	822098	21	A	P	39+3	G	4	2	10	15	V		R	F,3kg	No	A	No	
186	822385	20	B	M	39+4	G	3	…..	…..	….	C	FD	…..	M,2.7kg	Yes	B	Yes	E,F
187	822515	20	A	P	39+4	G	5	1	3	9	V		NR	M,3.4kg	No	A	No	
188	822229	28	B	M	39+2	G	5	1	3	8	V		NR	M,2.47kg	No	A	No	
189	822803	20	A	P	39+2	D	5	2	10	16	V		NR	M,1.8kg	No	A	No	
190	823017	21	B	M	40+4	A	3	…..	….	…..	C	POPP	….	M,3.4kg	No	A	No	A
191	823063	21	A	M	39+3	G	4	2	10	17	V		R	M,2.8kg	No	A	No	
192	823181	20	B	P	42+2	B	4	1	4	10	V		NR	M,2.6kg	No	A	No	
193	781638	21	A	P	41+3	A	5	2	11	18	V		R	F,3kg	No	A	No	
194	823901	21	B	M	39+4	G	3	2	9	12	V		NR	M,2.6kg	No	A	No	
195	767099	25	A	P	41+2	A	5	1	5	11	V		NR	F,3.2kg	No	A	No	
196	824527	30	B	M	41+0	A	3	…	…..	…	C	FD	….	F,3.3kg	Yes	A	No	
197	823558	20	A	P	40+0	C	4	2	9	14	V		R	F,2.5kg	No	A	No	
198	825096	26	B	M	41+4	A	5	1	4	10	V		NR	M,3kg	Yes	A	No	
199	824495	28	A	P	39+6	G	3	….	…..	….	C	FD	…	F,2.5kg	No	B	Yes	
200	808345	22	B	M	41+3	G	3	…	…..	…	C	FD	…	F,2.5kg	Yes	A	No	