COMPARATIVE STUDY OF CERVICAL RIPENING WITH SUBLINGUAL MISOPROSTOL AND INTRACERVICAL DINOPROSTONE GEL IN TERM PRELABOUR RUPTURE OF MEMBRANES

Dissertation submitted to

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MAY 2022

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This is to certify that the dissertation titled "**COMPARATIVE STUDY OF CERVICAL RIPENING WITH SUBLINGUAL MISOPROSTOL AND INTRACERVICAL DINOPROSTONE GEL IN TERM PRELABOUR RUPTURE OF MEMBRANES "** is a bonafide work done by **Dr.DHARINI M ,** Post graduate student,Department of Obstetrics and Gynaecology, **Thanjavur Medical college, Thanjavur – 04,** during the period **FEBRUARY 2021 TO NOVEMBER 2021** in partial fulfillment of rules and regulations of **The Tamilnadu Dr. M.G.R Medical University,** for the award of **M.D. Degree Branch II (Obstetrics and Gynaecology)** examination to be held in **May 2022.**

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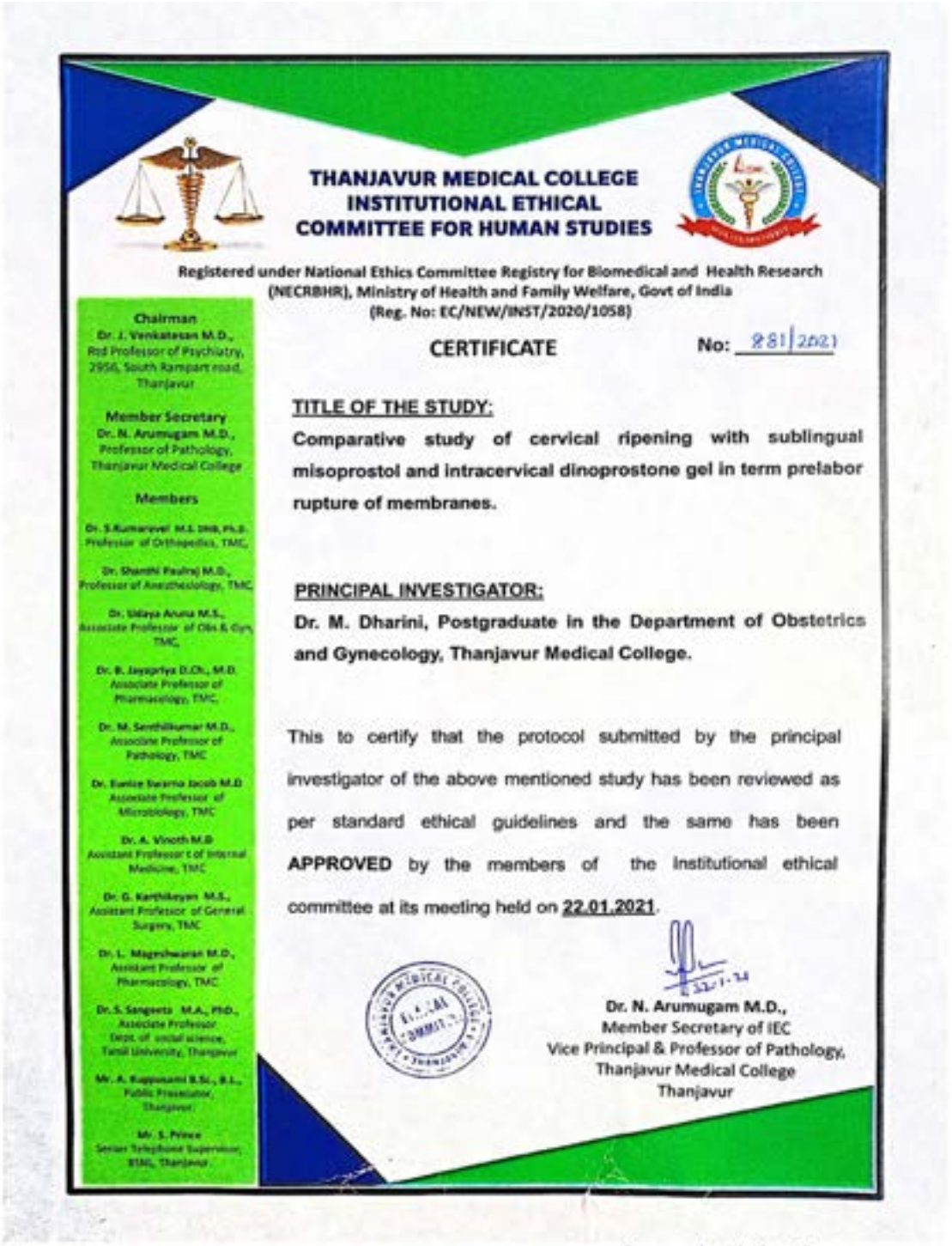

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TITLE OF THE STUDY:

Comparative study of cervical ripening with sublingual misoprostol and intracervical dinoprostone gel in term prelabor rupture of membranes.

PRINCIPAL INVESTIGATOR:

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This to certify that the protocol submitted by the principal investigator of the above mentioned study has been reviewed as per standard ethical guidelines and the same has been **APPROVED** by the members of the Institutional ethical committee at its meeting held on **22.01.2021**.

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DECLARATION

I solemnly declare that this dissertation titled **"COMPARATIVE STUDY OF CERVICAL RIPENING WITH SUBLINGUAL MISOPROSTOL AND INTRACERVICAL DINOPROSTONE GEL IN TERM PRELABOUR RUPTURE OF MEMBRANES "** was done by me at **the Department of Obstetrics and Gynaecology, Thanjavur Medical College, Thanjavur,** during year 2020-2022 under the guidance and supervision of **Prof. Dr. R.RAJARAJESWARI, MD., DGO., DNB.** This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of **M.D. BRANCH II (Obstetrics and Gynaecology).**

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I would be failing in my duty, if I don't place my sincere thanks to those patients who were the subjects of my study. Above all I thank God Almighty and my parents for immense blessings.

CONTENTS

ABBREVIATIONS

PROM Prelabour rupture of membranes

WHO. World Health Organization

PGE1. Prostaglandin E1

PGE2. Prostaglandin E2

LSCS. Lower segment cesarean section

BMI. Body mass index

CRP. C Reactive protein

ESR. Erythrocyte sedimentation rate

NICU. Neonatal intensive care unit

CONS. Coagulase negative staphylococcus aureus

AFI Amniotic Fluid Index

BPP. Biophysical profile

NST. Non stress test

RCT. Randomised controlled trial

AUC. Area Under the curve

FDA. Food & Drug Administration

NSAIDS. Non-steroidal anti inflammatory drugs

GIT Gastrointestine

PHC Primary Health Centre

GH. Government Hospital

INTRODUCTION

INTRODUCTION

Premature rupture of membranes(PROM) is defined as spontaneous rupture of fetal membranes that is chorioamniotic membranes before the onset of labour.

If membranes rupture after 37 completed weeks of gestation but before the onset of uterine contractions, it is defined as term PROM whereas rupture of membranes before 37 weeks is called preterm PROM.

Membranes rupture for more than 24hours before delivery is called prolonged premature rupture of membranes.

Incidence of PROM:

It complicates about 10% of all pregnancies. (according to Cochrane database review 2017 by Middleton P et al)[1]According to Indian studies(Bhalerao and Desai, 2000; Bhide, 2001), PROM occurs in 7-12% of labours. Spontaneous labour follows term PROM at 24, 48 and 96 hours in 70%, 85% and 95% of women respectively.[2]

The available management options in term PROM are expectant management that is waiting for the labour process to occur on its own and induction of labour. Even with plenty of studies regarding management options in term PROM, accurate diagnosis and management of term PROM is intriguing even in modern obstetrics and the management choices should be balanced in a double edged sword. As the time interval between rupture of membranes and delivery increases, chances of maternal and fetal complications such as chorioamnionitis, maternal sepsis, placental abruption, cord prolapse, increased chances for caesarean delivery, retained placenta, endometritis, postpartum hemorrhage and even maternal death, neonatal sepsis, neonatal intensive care unit admissions increase.

According to this, induction of labour within 6-12hours of membrane rupture in term PROM is advised, if woman is not in labour.This is to reduce the duration between rupture of membranes and delivery which is called latent period and it is especially important in those with unfavourable cervix (Middleton P et al) . Even view of women is more positive towards induction of labor in term PROM than expectant management (TERMPROM study by Hannah et al).[3]

Also WHO strongly recommends induction of labour in women with prelabour rupture of membranes at term as the quality of available evidence is very high[4.] Although oxytocin is the most commonly preferred agent for induction of labour in term PROM, in a subset of women with unfavourable cervix determined by Bishops score <6, prostaglandins do play a greater role.

When labour begins in a previously unfavourable cervix, cervical ripening is done to facilitate softening, thinning and dilation of cervix. This should be done to reduce failed induction as unfavourable cervix (according to Bishops score) at induction, increases the cesarean rates and also to decrease induction-delivery interval.

Mechanical methods of cervical ripening are relatively contraindicated in ruptured membranes as it further increases the chances of chorioamnionitis. Hence pharmacological methods of cervical ripening are advised in term PROM.

Pharmacological agents for cervical ripening include various formulations of prostaglandin such as prostaglandin E1, E2. A synthetic analogue of prostaglandin E1 which is called misoprostol has been used widely as an agent for cervical ripening. Routes of administration being include oral, sublingual and Intravaginal route. Misoprostol is available as a 100mcg(in scored) or a 200mcg tablet and for the purpose of cervical ripening, 25mcg or 50mcg is used by breaking the tablet.[5]

Greatest advantage of misoprostol usage lies in its storage in room temperature. There are 2 commercially available preparations of PGE2 for cervical ripening. 0.5mg of dinoprostone gel in a 2.5ml syringe and the other is a vaginal insert containing 10mg of dinoprostone. 0.5mg dinoprostone gel is used either intravaginally or intracervically. This study has been done to compare the safety and efficacy of sublingual misoprostol with intracervical dinoprostone gel for cervical ripening in term PROM.

AIM AND OBJECTIVES

AIM

To compare the safety and efficacy of sublingual misoprostol with intracervical dinoprostone gel for cervical ripening in term PROM.

OBJECTIVES

PRIMARY OBJECTIVE:

- To assess induction delivery interval.

SECONDARY OBJECTIVE:

- To assess women who entered into active phase of labour.
- To assess the duration of various stages of labour
- To assess the number of women who had failed induction (failure to have cervical changes 6 hours following induction and also includes those who failed to establish adequate uterine contractions even after 24hours of induction/complete doses of induction).
- To assess the complications of induction like uterine hyperstimulation.
- To assess women who need Cesarean section.
- To assess maternal complications like infection (chorioamnionitis/endometritis) and neonatal outcome.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Comparative study of cervical ripening with sublingual misoprostol and intracervical dinoprostone gel in term pre labour rupture of membranes

Rupture of membrane:

During pregnancy, a fluid-filled sac called the amniotic sac surrounds and protects the fetus. When a tear or hole happens in the sac, it's called rupture of the membranes, which is commonly described by the women as breakage/ leakage of waters.

If it happens spontaneously, it is called spontaneous rupture of the membranes and it most commonly happens once active labour has started. But sometimes the membranes may rupture by doctor or midwife to start or to speed up labour which is termed as artificial rupture of the membranes (ARM). ARM is done to accelerate the labour process as it increases the frequency and intensity of uterine contractions by further increasing the release of prostaglandins and also oxytocin.

Sometimes the membranes, amniotic sac break before a woman goes into labor. When the water breaks early, it is called premature rupture of membranes (PROM). Most women will go into labor on their own within 24 hours. If the water breaks before the 37th week of pregnancy, it is called preterm premature rupture of membranes (PPROM).

RISK FACTORS FOR PROM

In most cases, the exact cause of PROM is unknown.

Some risk factors may be:

- Infections such as chorioamnionitis, urinary tract infection and lower genital tract infections
- Too much stretching of the amniotic sac as in multiple pregnancy or polyhydramnios
- Any previous surgeries or biopsies of the cervix
- Previous history of PROM or PPROM
- Cervical incompetence
- Smoking
- Dietary habits
- Coitus
- Placental pathology

In lower genital tract infections, organisms involved in it cause activation of phospholipase A2 & C enzymes by ascending to the membranes, thereby increasing the production of prostaglandins, leading to increased uterine contractions. Also the organisms cause weakening of amnion by the release of protease, collagenases, elastases.

Some of the organisms involved in chorioamnionitis are:

- Group B streptococcus
- Staphylococcus aureus
- Neisseria gonorrhoea
- Chlamydia
- E coil and
- Organisms causing bacterial vaginosis.

Previous history of PROM and BMI <20 were considered significant risk factors for PROM by Kovavisarach et al (2000).

Dietary deficiencies of ascorbic acid, zinc, vitamin E, copper cause defect in the membranes thereby leading to PROM. This was studied by Woods et al in 2001.

Smoking and excessive coffee consumption is also associated with PROM which was analysed by Williams et al in 1992.

DIAGNOSIS OF PROM

HISTORY

Usually PROM is diagnosed with the patient history of sudden gush of fluid followed by persistent leak. Though history is accurate in the diagnosis of 90% of cases of PROM, sometimes additional examination and investigations are needed to confirm the diagnosis of PROM.

SPECULUM EXAMINATION:

Speculum examination under aseptic precautions to look for any pooled fluid in the posterior fornix and also for leakage of fluid through the cervical os confirms the diagnosis. Speculum examination was sufficient in most women and it provides all the information provided by a digital examination as studied by Manson A Laurel et al in 1985.

If there is no pooled fluid in the posterior fornix or no active leakage through the os, it's better to diagnose PROM by asking the patient to cough or strain (valsalva manoeuvre). Sometimes fluid leakage or pooling won't be demonstrated even by Valsalva and at that time, patient will be advised to keep a sterile pad for sometime and observed later for leakage of fluid.

PerVaginal examination should be done at the time of admission to assess cervical status and should be minimised in order to reduce the chances of introducing microorganisms while doing pv and should be done afterwards, only when it is indicated .

INVESTIGATIONS:

If the ruptured membranes was not diagnosed with history and examination alone, certain techniques were developed for it which includes

1. pH determination
2. Arborization or ferning pattern
3. Identification of lanugo hair,
4. Identification of fetal cells
5. Dye test
6. Detection of fetal fibronectin, alpha feto protein and insulin like growth factor binding protein-1[6]

1) pH determination:

Concept behind this is pH of vagina is acidic 5.2 -6.0 while amniotic fluid is alkaline with pH of 7.0-7.7 and once with the rupture of membranes, vaginal pH will change to 6.0-8.1.

Many colorimetric methods are available for the demonstration of hydrogen ion concentration in the vagina which includes

a. Litmus paper test:
   - Red litmus turns to blue on contact with amniotic fluid.
   - It is very easy and quick to perform
   - Rate of false positives is 35% in the contamination of blood, semen, urine and infection
b. Bromothymol blue test: changes from orange to blue-green colour at pH6.0-7.6
c. Nitrazine test:

Nitrazine paper comes in the form of amnicator sticks and these sticks was directed towards pooled fluid in posterior fornix or else to swab the posterior fornix, if there is no pooling. Amnicator strips change from orange to dark blue colour at a pH of 6.4-6.8 and this is interpreted as a positive test for ruptured membranes.

2) Arborization or ferning pattern:

A drop of fluid pooled in the posterior fornix or leaking through the cervical os is placed on a glass slide and air dried for demonstration of crystallisation of amniotic fluid which resembles palm leaf pattern and hence it is called ferning. Ferning occurs due to the presence of sodium chloride in the amniotic fluid and this ferning is unaffected by the presence of blood or meconium. Hence accuracy of this method for diagnosing PROM is

high. Pooling of fluid in the posterior fornix, nitrazine and ferning together constitutes combined traditional diagnostic test (CTDT)[6,13]

3) Identification of lanugo hair:

Lanugo hair in the amniotic fluid is demonstrated by microscopy

4) Identification of fetal cells by Nile blue sulfate test:

On staining with 0.1% Nile blue sulfate, exfoliated fetal cells stain orange brown

5) Dye test:

It is an invasive test and it involves intraamniotic administration of dyes like indigo Carmine, Evans blue and demonstration of staining of the pad.Though it is invasive, intra-amniotic instillation of dye continues to be the gold standard for diagnosing ruptured membranes.

6) Detection of fetal fibronectin (fFN):

Detection of fetal fibronectin is very accurate because fetal fibronectin is a glycoprotein that is present only in the amniotic fluid.Fetal fibronectin is very significant in PPROM for diagnosing preterm birth.

7) Detection of alpha feto protein:

Alpha feto protein in the amniotic fluid is demonstrated by various kits employing colorimetric monoclonal antibody test. It is produced by fetal liver and yolk sac and is present in the amniotic fluid throughout gestation. Though it is very accurate, it is not useful if the duration of PROM exceeds 24 hours.

8) Detection of placental alpha micro globulin -1 (PAMG-1)

PAMG-1 is a glycoprotein that is synthesised and released by cells lining the uterus into the amniotic fluid throughout pregnancy. Hence concentrations of PAMG-1 is very much higher in amniotic fluid(2000 -25000 ng/ml) than blood(0.05-0.2 ng/ml) and in

cervicovaginal secretions, its concentration is much lower than in blood and hence its presence in cervicovaginal secretions indicates ruptured membranes.[7]

Using immunoassay methods (Amnisure),PAMG-1 in cervicovaginal secretions is detected and it has got a sensitivity of 97.2%, specificity of 69% and 100% positive predictive value, and 75% negative predictive value for the diagnosis of presence of amniotic fluid in the vagina.[8]

It gives results within minutes and it is a bedside strip test but it is very costlier[9]. PAMG-1 immunoassay was found to be superior & accurate to other conventional diagnostic methods of PROM and IGFBP-1 immunoassay in invitro studies.[10] Same principle is employed in Partosure TTD (Time to delivery) which predicts the time to delivery in case of women with PPROM.

9) Detection of insulin-like growth factor-binding protein-1 (IGFBP-1):[11]

IGFBP-1 is a major protein that is detected throughout pregnancy in the amniotic fluid. It is synthesised by the decidua and fetal liver. IGFBP-1 concentration in maternal serum increases with gestational age but in amniotic fluid, its concentration is always 100-1000 fold higher than that in maternal serum and it is undetectable in cervicovaginal secretions unless there is rupture of membranes. Hence its detection using monoclonal antibodies (Actim PROM test) is used in the diagnosis of PROM. It is simple, easy, rapid and results are not affected by contamination with non amniotic body fluids[12.] Though it is efficacious, it is usually considered as a complementary test for the diagnosis of PROM.

INVESTIGATIONS:

1) COMPLETE BLOOD COUNT:

For baseline heemoglobin, total lecocyte count, platelet count. It should be repeated once in 12hours for monitoring total leukocyte count Elevated leukocyte count gives an hint about systemic infection though it is very nonspecific.

2) C-REACTIVE PROTEIN:

It is an acute phase protein that is synthesised by the liver during infection[14.] It also accompanies both acute and chronic inflammatory disorder.

It's main role is to identify potentially toxic autogenous substances released from damaged tissues ant to detoxify them by binding with them and removing them from blood.

In patients with intrauterine infection, CRP is found in elevated levels in both peripheral circulation and in the amniotic fluid and hence it is used as an early predictor of chorioamnionitis.[15]

CRP is detected in the blood either by immunochemical methods such as laser nephelometry or by sensitive homogenous enzyme assay.

CRP in plasma greater than 15mg/l (1.5mg/dl) correlates well with amniotic fluid interleukin levels of greater than 1500pg/ml.[16] Also values greater than 15mg/l showed a significant a highly significant correlation with positive amniotic fluid culture.[17]

Sujata et al,2016 showed that only CRP determination accurately reflects chorioamnionitis and elevated CRP levels correlate better with histopathological evidence of chorioamnionitis than with clinical features[18]. It is highly sensitive for the prediction of sub clinical chorioamnionitis

3) ERYTHROCYTE SEDIMENTATION RATE:

ESR is increased with normal pregnancy and also during significant infection and inflammmation. Hence ESR is also elevated during intraamniotic infections

Amirabi et al, 2012 found ESR cut off value of 52 to be 66.7% sensitive, 60% specific to diagnose chorioamnionitis and ESR diagnostic value was minimally acceptable for diagnosing chorioamnionitis in women with PROM

4) MATERNAL PLASMA CYTOKINE PROFILE:

Maternal plasma concentrations of several inflammation-related cytokines is found to be significantly elevated in clinical chorioamnionitis . But for the diagnosis of bacteria in the amniotic cavity, maternal plasma cytokine concentrations have limited value (Roberto Romero et al, 2015).[19]

But a model comprising a combination of certain maternal characteristics and maternal serum levels of IL-6 proves to be a good non-invasive predictor of histological chorioamnionitis according to Portilla et al,2018 [20]

5) HIGH VAGINAL SWAB FOR CULTURE:

It should be taken before doing per vaginal examination and administration of antibiotics. There is a positive correlation between high vaginal swab culture positivity and neonatal sepsis[21.]

Maternal symptoms alone cannot identify all infected infants. This is because, when the mother has abnormal bacterial colonisation of the urogenital tract, an ascending but silent amniotic fluid infection, or symptomatic chorioamnionitis, early onset bacterial infections in the newborn may occur. Incidence of neonatal infections among infants born to PROM mothers is 1-2.6%[22]. Organisms most commonly isolated from high vaginal swab were E.coli and Staphylococcus aureus especially CONS.[23]

6) AMNIOTIC FLUID ANALYSIS:

Amniocentesis is done for the withdrawal of amniotic fluid and cultured for the diagnosis of intrauterine infection. It is invasive and requires prolonged time for results.

Hence amniotic fluid gram stain has been done to evaluate the presence of leukocyte and bacteria. Since these tests are invasive, they are replaced by rapid diagnostic tests.

7) ULTRASOUND EXAMINATION :

- To confirm fetal presentation, fetal heart sounds,
- To estimate AFI- amniotic fluid index
- To assess fetal growth
- Fetal biophysical profile to document well being of the foetus. Absent fetal lung movements in BPP indicates chorioamnionitis
- Use of fetal biophysical profile improves pregnancy outcome in premature rupture of membranes. Use of persistently low BPP (7 or less on 2examinations two hours apart) as an indication for delivery improves maternal and neonatal infection in the management of premature rupture of membranes.

8) NON STRESS TEST:

- NST should be done to assess the fetal well being before proceeding for further management.
- Intrauterine infections can be predicted by fetal heart rate variations in NST
- Nonstress test is 78.1% sensitive and 86.3% specific in predicting infection outcome in patients with PROM in a study conducted by Anthony M et al in 1986.

COMPLICATIONS OF PROM

MATERNAL COMPLICATIONS:

1) IMMEDIATE THREATS

When rupture of membranes happen, there are chances of immediate threat such as cord prolapse, placental abruption.

Incidence of placental abruption in PROM is approximately 6% which is significantly higher than the rest and hence vaginal bleeding in the presence of PROM should be evaluated with caution.

2) FEBRILE MORBIDITY:

It's occurrence increases with increased latency period or prolonged labour or with the development of chorioamnionitis or overt infection of the amniotic cavity.

3) CHORIOAMNIONITIS:

Bacterial infection or inflammation of the fetal amnion and chorion membranes is called chorioamnionitis and it occurs more frequently in women with PROM. Ultimately it can lead to intrapartum, postpartum sepsis and septicaemia.

In a randomised controlled trial by Evelina Chapman et al, 2014 , 1-2% of term births and 5-10% of preterm births are complicated by clinical chorioamnionitis whereas 20% of term births and 50% of preterm births are complicated by sub clinical chorioamnionitis.[24]

It is also known as triple I: intrauterine inflammation or infection or both.

Signs and symptoms of chorioamnionitis:

1) maternal fever (intrapartum temperature >100.4 F or > 38C
2) Baseline fetal tachycardia
3) Maternal leucocytosis in the absence of corticosteroids (Total leukocyte count

>15,000 cells/mm

4) Definite purulent fluid from the cervical os.

5) Maternal tachycardia and uterine tenderness are de-emphasised for the diagnosis of chorioamnionitis .[25]

Clinical chorioamnionitis in pregnancy is diagnosed based on the presence of fever with atleast 2 other conditions such as fetal tachycardia, maternal leucocytosis, or purulent fluid coming from the cervical os, maternal tachycardia, uterine tenderness.

In case of histologic chorioamnionitis, maternal signs and symptoms of infection are absent and hence it is called silent chorioamnionitis and it is diagnosed based on the presence of polymorphonuclear leukocyte infiltration of the chorioamnion.

Diagnosis:

Though the diagnosis of chorioamnionitis in pregnancy is mainly clinical, certain laboratory tests such as white blood cell count (WBC) , CRP levels, serum interleukin -6 or ferritin levels and also the amniotic fluid analysis for leukocyte count, gram staining, pH, cultures aid in the diagnosis of chorioamnionitis.

Management:

- Early delivery
- Supportive care
- Antibiotic administration

Antibiotic regimens used in the treatment of chorioamnionitis include the following:

1) Ampicillin and gentamicin (standard)[26]
2) Clindamycin or metronidazole when endometritis is suspected (post delivery)
3) In case of penicillin-allergic patients, vancomycin
4) Mono therapy with ampicillin-sulbactam, ticarcillin-clavulanate, cefoxitin, cefotetan, or piperacillin-tazobactam can also be used.

Ampicillin covers GBS, Haemophilus species, many enterococcus strains and Listeria monocytogenes. Gentamicin provides broad spectrum coverage against gram- negative bacteria. For anaerobic coverage, metronidazole may be used.

These antibiotics are administered only in the intrapartum period when the mother is having fever. After vaginal delivery, no additional doses are needed but one additional dose is needed after cesarean delivery.

Complications:

Maternal- dysfunctional labour

Postpartum hemorrhage

Endometritis

Peritonitis

Sepsis

Adult respiratory distress syndrome

Rarely, maternal death

Fetal - Neonatal sepsis,

Pneumonia

Meningitis and

Death

4) MATERNAL SEPSIS:

Organ dysfunction due to infection during pregnancy, childbirth, post abortion, or postpartum period leading to a life-threatening condition is defined as maternal sepsis according to WHO.[27]

Maternal sepsis can happen in intrapartum or postpartum period and only 5% mothers with chorioamnionitis will develop sepsis whereas 10-20% of the babies will develop infection.

5) POSTPARTUM HEMORRHAGE & RETAINED PLACENTA:

PROM remains one of the risk factors for uterine atony and retained placenta, hence PPH is more common among mothers with PROM

6) FAILED INDUCTION

In a study conducted by Swati Pandey et al[28], 100 PROM mothers at 28-42weeks of gestation with no additional medical or obstetrical complications were taken as cases with 100 normal deliveries as controls. Incidence of PROM was 7.71% according to PROM. Incidence of LSCS(31%) and other abnormal deliveries were high, compared to controls. And fetal distress (45%) , failed oxytocin induction (16%) were the commonest indications for LSCS in this study.

In another study by Sridevi et al in 2018[29], 100 PROM patients were studied and it was found that PROM was more common in primigravidas and incidence of LSCS was higher -27% among study group with non-reassuring fetal status(29.6%) and h/o previous LSCS(22.2%) were the commonest indications for LSCS.

In another study by Sailaja et al in 2017[30], LSCS rate was 27.5% and it was more common in primigravidas with failure to progress being the commonest indication followed by fetal distress.

Priya Nair et al in 2020[31] studied the maternal and fetal outcome following term prelabor rupture of membranes in a peri urban tertiary care centre & found LSCS rate to be 44.59% with majority of them being primigravidas and fetal distress secondary to misoprostol induction being the commonest cause followed by failed induction.

FETAL COMPLICATIONS:

1) Neonatal sepsis
2) Perinatal asphyxia
3) Fetal distress

4) Low Apgar score
5) Perinatal mortality

In a study conducted by Abirami et al in 2020[32], it was found dat incidence of term PROM was 14% which was common among primigravidas. 73.6% had induction followed by acceleration , 50.81% delivered vaginally whereas 49.19% delivered by LSCS. 18.7% newborns were admitted in NICU with respiratory distress syndicate being the commonest reason for admission . Neonatal mortality was 0.4% whereas 32% babies had low birth weigh and this was attributed to the coexisting maternal comorbidities like PIH, anemia and BOH.

Shruthi Gupta et al in 2019[33], in their prospective study on 200 pregnant women with PROM at or near term, it was found that neonatal complications increased with an increasing latent period especially neonatal sepsis and hence it was concluded that pregnancies with PROM at and near term shouldn't be managed expectantly and the prevalence of specific neonatal complications was NICU admission (26%), birth asphyxia(8%), neonatal sepsis(4%) and neonatal mortality(2%).

In a study conducted by Arpita A. Jaiswal et al in 2017[34] which is a prospective study conducted over a period of 18 months for maternal and fetal outcomes in premature rupture of membranes in central rural India, maternal morbidity was 26% with clinical chorioamnionitis being the commonest and perinatal morbidity in 30% cases with the commonest being early onset neonatal infections and birth asphyxia leading to 1.43% perinatal mortality .

In the study of maternal and fetal outcomes in term premature rupture of membranes by Tigist Endale et al in 2016 [35], about 33.5% neonates experienced unfavourable outcomes with birth weight less than 2500g being the commonest.

MANAGEMENT OF TERM PROM:

There are arguments regarding whether to wait after PROM for spontaneous labour onset or to start the induction process.

As the duration of complications especially neonatal complications increase with the duration of latency, it is better to avoid expectant management.

TERMPROM study group by Hannah et al[3] in 1996 is the hall mark study in women with prelabour rupture of membranes at term that concluded that immediate induction of labour with oxytocin or vaginal prostaglandin E2 gel and expectant management for upto 4days followed by induction, result in similar rates of neonatal infection and cesarean section. But intravenous oxytocin induction do lower the risk of maternal infection than expectant management. Even women view induction of labour more positively than expectant management.

In a 2006 Cochrane analysis by Philippe Middleton , Emily Sheperd [1]et al that reviewed the advantages of early intervention with either oxytocin or prostaglandins or expectant management in the setting of term PROM, it was concluded that oxytocin should be considered before expectant management .

In another cochrane analysis of RCTs in 2017 [36] comparing planned early birth with expectant management in women with PROM at 37weeks gestation or later it was concluded that evidence was very low to suggest that planned early birth (with induction methods such as oxytocin or prostaglandins) did reduce the risk of maternal infectious morbidity compared with expectant management for PROM at 37weeks gestation or later, without an apparent increased risk of cesarean section.

Anjali Gupta et al in 2018[33] conducted a prospective study on 100 PROM women and compared the maternal and perinatal outcome of early induction with expectant management. It was concluded that women with termPROM can be given informed

choice of expectant management and early induction explaining the merits and demerits of both options since neonatal sepsis was seen more in expectant group though statistically insignificant (22% versus 16%) and also fetal distress & LSCS were comparatively higher in induction group (16% vs 2%).

In another prospective study conducted by Sachin Wankhede et al[37] to study the effectiveness of maternal and fetal outcome in term pregnancy with early induction of labor with cervical PGE2 versus expectant management, it was concluded that early induction of labor in cases of PROM at term with PGE2 gel results in reduction of latency of labour but also increased operative intervention and expectant management has greater maternal and neonatal morbidity.

In a comparative study to assess the effectiveness of early labor induction with Cervical prostaglandin E2 versus expectant management in term PROM women by Yogesh Neena et al [38] in 2013 it was concluded that induction with prostaglandin in cases of term PROM shortens delivery interval and maternal hospital stay with reduction in maternal- neonatal sepsis. Rate of cesarean section remained almost same. The same was concluded in a study by Krupa Shah et al in 2012.[39]

In a hospital based comparative study involving women with term PROM, immediate induction was compared with that of delayed induction after 12hours of PROM, it was concluded that delayed induction after a waiting period of 12 hours stands as a reasonable option in term PROM Anand it decreases the the number of operative deliveries without compromising the maternal and neonatal outcome. This was conducted in 2017 by John Mary Betty Agnes et al.[40]

Hence it is concluded that immediate induction offers maternal and neonatal benefits than expectant management.

UNFAVOURABLE CERVIX:

Certain women with term PROM will have unfavourable cervix which takes much longer time for delivery even with oxytocin induction which in turn increases the latency period leading to increased maternal and neonatal complications.

So In order to hasten the delivery cervical ripening is done before oxytocin induction.

CERVICAL RIPENING PHYSIOLOGY :

In a previously unfavorable cervix, when dilatation occurs on the onset of labour, then it is termed as cervical ripening. Cervix is an imminent part and comprises of two types of collagens. Of the two types major component is type I collagen (66%) and the rest 34% is type II collagen. These collagen bundles are in close knit with the proteoglycans provide the firm consistency to the cervix.

The firmness is also been provided by dermatan sulphate and Chondroitin sulphate which are glycosaminoglycans also add to the firmness. The orientation of the collagen fibers also add to the firmness of cervix. The cervix which is this firm in nonterm women becomes soft during labour which is brought in by the collagenase enzyme. This collagenase is secreted by fibroblasts and leucocytes and the level of this collagenase increases towards term.

The precursor for this collagenase enzyme is Procollagenase which is produced by the prostaglandin. Thus it helps in ripening of cervix. The factors that also contribute to cervical ripening are:

Changes in glycosaminoglycans:

This acts by increasing the water content in the cervix thereby loosening the collagen fibers which also increases the production of immature collagen.

1. Inflammatory mediators and Enzymes like collagen:

These act by assessing the collagen breakdown.

Thus along with these factors, which act on collagen and bring in breakdown of collagen thereby decreasing the firmness of cervix which is what happens towards term.

Steps in Cervical Ripening

Glycosaminoglycans which are hydrophobic

⇩

Hyaluronic Acid hydrophilic

⇩

Water imbibition

⇩

Collagen fibrils destabilize

⇩

Cervical Ripening

Cervix is firm in early pregnancy becomes soft in prelabour and dilatation happens during labour. On the contrast Myometrium, quiescent in early stages of pregnancy becomes excitable during prelabour and becomes contractable when in labour.[17]

Favorability of the cervix is assessed by Bishop scoring system.

BISHOP SCORING SYSTEM [41]

SCORE	DILATATION (cm)	POSITION OF CERVIX	EFFACEMENT (%)	STATION	CERVICAL CONSISTENCY
0	Closed	Posterior	0-30	-3	Firm
1	1-2	Mid Position	40-50	-2	Medium
2	3-4	Anterior	60-70	-1, 0	Soft
3	5-6	-	80	+1, +2	-

The original Bishop score which was suggested by Bishop was modified by Calder. Calder modified the original Bishop score in 1974 which is called the modified Bishop score. In the modified Bishops score the 'effacement of cervix' was changed to length of cervix for scoring.

Modified Bishop score less than 6 is considered to be unfavourable and it indicates that prior cervical ripening is needed before labour induction for successful vaginal delivery.

METHODS OF CERVICAL RIPENING:

1) Mechanical
2) Pharmacological

Mechanical methods of cervical ripening are contraindicated in PROM since it increases the chances of chorioamnionitis and sepsis

MISOPROSTOL:

Misoprostol is a synthetic analogue of PGE1(15-deoxy-16-hydroxy16-methyl PGE1) It is commercially called as CYTOTEC.[42] It is initially approved by US-FDA for the prevention and treatment of acid peptic disease in patients receiving no steroidal anti-inflammatory agents. Misoprostol is structurally modified to enhance its oral bio activity, safety and duration of anti secretion action by transferring hydroxyl group from C15 to C16 and by adding methyl group.

Greatest advantage of misoprostol is its low cost and storage in room temperature.

Misoprostol is used off-label for a variety of indications in the practice of obstetrics and gynecology, including medical abortion, medical management of miscarriage, induction of labor, cervical ripening before surgical procedures, and the treatment of postpartum hemorrhage.

Pharmacokinetics

Routes of misoprostol administration include oral, vaginal, sublingual, buccal, or rectal. Pharmacokinetic studies comparing oral and vaginal administration have shown that vaginal misoprostol is associated with slower absorption, lower peak plasma levels, and slower clearance, similar to an extended-release preparation. Vaginal misoprostol is also associated with a greater overall exposure to the drug (area under the curve [AUC]) and greater effects on the cervix and uterus. There is, however, a wide variation in the absorption of misoprostol through the vaginal epithelium among different women. The rectal route of administration shows a similar pattern to vaginal administration, but has a lower AUC, including a significantly lower maximum peak concentration.

The sublingual route of administration has an AUC similar to vaginal administration, but more rapid absorption and higher peak levels than either vaginal or oral administration. This translates into higher rates of gastrointestinal side effects. Nevertheless, the sublingual route also causes uterine contractions at a rate equivalent to vaginal administration and has less variation in absorption.

The buccal route of administration shows a lower AUC, a lower peak concentration, and fewer side effects than sublingual administration. The buccal route has a pattern of absorption similar to the vaginal route, but produces lower serum levels overall. Nonetheless, the buccal and vaginal routes of administration have similar effects on uterine tone and activity. The buccal route of administration is also thought to be the least variable in terms of drug exposure and peak levels.

Absorption of misoprostol after its administration orally is rapid and then is rapidly deesterified to form misoprostol acid which is the principal and active metabolite of the drug. Misoprostol absorption is reduced by food and antacids resulting in delayed and decreased peak plasma concentrations of the active metabolite.

Excretion of free acid is mainly via urine with an elimination t1/2 of 20-40minutes.

The administration of NSAIDs for pain relief does not alter the efficacy of misoprostol. There are no known drug interactions with misoprostol.

Adverse effects:

Misoprostol's side effects are dose dependent and include diarrhoea, with or without abdominal pain and cramps occur in upto 30% of patients. others include nausea, vomiting, fever, and chills, uterine contractions, uterine hyperstimulation and rarely, uterine rupture .

Tachysystole that is more than 5contractions in a 10minute period averaged over 30mins with or without FHR changes is more common with vaginal misoprostol than vaginal/ intracervical PGE2 and oxytocin. And these complications appear to be dose dependent with lower rates of uterine tachysystole with FHR changes is seen with lower dosages of misoprostol (25mcg every 6hours versus every 3hours).

Availability:

Misoprostol tablet is available as a 100mcg (unscored) or a 200mcg tablet. Initial dose for cervical ripening and labor induction should be one quarter of an unscored 100mcg tablet and the frequency of administration should be more than every 3-6hours.

Teratogenicity

Misoprostol is considered a teratogen. Congenital defects following prenatal exposure in early pregnancy to misoprostol include skull defects, bladder exstrophy, arthrogryposis, cranial nerve palsies, facial malformations, terminal transverse limb defects, and Moebius sequence. This constellation of congenital malformations is thought

to be due to a vascular disruption secondary to uterine contractions caused by misoprostol. The absolute risk of congenital malformations after prenatal exposure to misoprostol is estimated to be approximately 1%.

Pharmacokinetic studies reveal that misoprostol is excreted into breast milk with drug levels that rise and fall very quickly. Levels become undetectable within 5 hours of maternal ingestion. However, breastfeeding women should be advised that misoprostol may cause infant diarrhea.

- Misoprostol is an effective cervical ripening agent prior to first-trimester surgical abortion. It is recommended especially for women between 12 and 14 weeks of gestation, adolescents, and for women in whom cervical dilation is expected to be difficult either due to patient factors or provider inexperience.

- Misoprostol for cervical ripening as a substitute for laminaria prior to second trimester dilation and evacuation is only recommended under 16 weeks of gestation.
- Misoprostol is an effective cervical ripening agent in premenopausal women prior to hysteroscopy. The greatest benefit is seen in nulliparous women and for operative hysteroscopy. Whether the routine use of misoprostol prior to hysteroscopy is beneficial is still unknown.
- Misoprostol for cervical ripening prior to gynecologic procedures in postmenopausal women has not been found to be effective.
- Misoprostol is an option for the management of early pregnancy failure and incomplete abortion in women who are hemodynamically stable without signs of infection. A single dose of 800 μg vaginally is typically used.
- Misoprostol is a proven induction agent in the second trimester for termination of

pregnancy or fetal death. One regimen is 200-400 μg vaginally every 6 hours up to 48 hours.

Cervical Ripening and Induction of Labor With a Viable Fetus

Misoprostol is not USFDA approved for induction of labor and cervical ripening.

Compared with placebo, misoprostol causes cervical ripening before induction with oxytocin. When used for cervical ripening, misoprostol can be administered orally, sublingually, or vaginally, although there is more evidence for vaginal regimens. A commonly used dose is 25 μg administered vaginally every 4 hours as needed, with a maximum dose of 150 μg.Doses are withheld if contractions are more frequent than every 4 minutes. Electronic fetal heart rate monitoring is used to evaluate fetal status 20 minutes before administration and continued for 4 hours after each dose.

In a meta analysis conducted by Monique G Lin in 2005 [43] which evaluated RCTs evaluating the safety and efficacy of PGE1 in comparison with placebo or expectant management and oxytocin, it was concluded that misoprostol is an effective and safe agent in induction of labour in term PROM . Compared with oxytocin, the rate of maternal and neonatal complications, contraction abnormalities were similar in both the groups.

In a cochrane systematic review conducted by Robbie et al in 2021[44]to assess the safety and efficacy of low dose oral misoprostol for labour induction with viable fetus in third trimester of pregnancy, it was concluded that low-dose misoprostol when compared with vaginal dinoprostone had fewer cesarean sections, lower rates of hyperstimulation but the time to delivery is increased. Oral administration of low dose misoprostol orally rather vaginally had similar rates of vaginal birth, very less chances of hyperstimulation associated with fetal heart rate abnormalities and fewer cesarean sections because of fetal

distress and it supports the use of low dose oral misoprostol with the starting dose of 25micrograms since it offers a good balance of efficacy and safety.

Optimal dosing of misoprostol that will achieve effective induction without uterine hyperstimulation and resultant fetal heart rate changes has been the topic of many studies. As with cervical ripening, an effective dose of misoprostol without high rates of uterine hyperstimulation is 25 μg administered every 4 to 6 hours.

INTRACERVICAL DINOPROSTONE

Prostaglandin E2 (PGE2) gel, also known as dinoprostone, is a naturally occurring compound involved in promoting labor, though it is also present in the inflammatory pathway.

Prostaglandin E2 is FDA approved for cervical ripening for the induction of labor in patients for whom there is a medical indication for induction.

Intracervical dinoprostone gel is placed inside the cervix, but not above the internal os. It can be repeated after 6-8hrs , to a maximum of 3doses in 24 hours.

When used as a vaginal pessary, it is indicated as an abortifacient from gestational week 12 to 20 or for the evacuation of uterine contents for the management of missed abortion and intrauterine fetal death up to 28 weeks.

Mechanism of action

Prostaglandin E2 causes contractions in the myometrium via direct stimulation. It binds to G protein-coupled receptors (GPCRs) EP1-4 that lead to a variety of downstream events depending on the EP subtype and cell-type-specific expression patterns.

Prostaglandin E2 also promotes cervical dilation, effacement, and softening, similar to the natural progression of pregnancy, possibly due to increased collagenase secretion.

Administration

PGE2 is administered as cervical gel or vaginally as a suppository, gel, or insert. The endocervical gel and vaginal inserts are agents for cervical ripening induction. The cervical gel has a more rapid release than the vaginal insert but might be less convenient, as the procedure requires more vaginal examinations.

After administration, patient should remain in the supine position for 30minutes.

However, drug administration should cease if there are no contractions within twenty-four hours after maximal dosing or if there are severe adverse effects, including membrane rupture or uterine hyperstimulation.

Adverse Effects

The most common side effects of prostaglandin E2 are on gastrointestinal smooth muscle. The suppository correlates with the most severe side effects, with two-thirds of patients experiencing vomiting, two-fifths experiencing diarrhea, and one-third experiencing nausea. Other adverse effects include temperature elevation in half of the patients, headache in one-tenth, and shivering and chills in one-tenth. Anti-emetics and anti-diarrheal medications may be necessary before and during the drug administration to counteract these side effects.

The insert and gel have a less than one percent incidence of gastrointestinal symptoms. However, studies have shown that there are links to a higher chance of uterine hyperstimulation with and without fetal distress (greater than 2%) versus placebo (under1%). Additionally, they also have an increased chance of fetal distress without uterine hyperstimulation (over 2%) versus placebo (1%). There were also associated fetal

heart rate changes, with and without distress. Unfortunately gel cannot be removed but inserts can be removed once there is hyperstimulation and in case of gel, rescue tocolysis with subcutaneous terbutaline 250mcg.

Contraindications of prostaglandins:

Prostaglandins are contraindicated in patients with a known hypersensitivity to it. It should be avoided in situations in which vaginal delivery or the induction of labor is contraindicated . Its use for cervical ripening are contraindicated in patients with fetal distress where delivery is not imminent or who have vaginal bleeding during pregnancy, marked cephalopelvic disproportion, and/or multipara with six or more previous term pregnancies. Prostaglandins for labor induction should also be avoided in patients with a history of asthma, glaucoma, or heart disease.

In addition to this, misoprostol causes clinical exacerbation of inflammatory bowel disease and should be avoided in this condition.[42] Misoprostol usage is contraindicated in those who had previous cesarean section or other uterine surgery because of the risks of hyperstimulation and uterine rupture, especially in the third trimester.

Oxytocin should be administered atleast 4hours after the last application of misoprostol and atleast 6hours after the last application of PGE2.

Monitoring after prostaglandins administration:

Prostaglandins administration should only take place in a double setup with NICU care setting under clinician supervision. A nonstress test is recommended before its administration.

Temperature, pulse, respiratory rate, blood pressure, uterine activity, fetal status, and progression of cervical dilation, vaginal bleeding all require monitoring immediately after prostaglandins administration followed by hourly for 4-6 hours.In particular, the healthcare team should look for any signs of uterine hyperstimulation, sustained uterine contractions, and fetal distress. Upon entry into active labour, more frequent intermittent fetal heart rate monitoring/ continuous electronic monitoring should be done. If these or any other adverse effects present, patient should be resuscitated with intravenous fluids, tocolytics preferably betamimetics. If associated with abnormal fetal heart rate pattern, delivery should be accomplished.

A study conducted by Oza et al [45] in the Department of Obstetrics & Gynaecology, Ahmedabad for the comparison of PGE1 and PGE2 for induction of labour in premature rupture of membranes at term in 2016 had compared the outcome of induction in terms of parity, induction delivery interval, maternal and fetal complications in termPROM. 100 termPROM women were selected and randomly divided into two groups for induction. Good number of patients delivered vaginally in both the groups and induction delivery interval is shorter with misoprostol group but it was associated with hyperstimulation, fetal distress and postpartum hemorrhage more than dinoprostone gel. So, tab misoprostol is not a safer drug where continuous monitoring of women is not available. Also women who had given aggressive management had less chances of chorioamnionitis, neonatal infection and less hospital stay.

Another study conducted by Anjali Gupta, Vijaya Kumari in 2015 [33] compared the efficacy of prostaglandin E1 tablet versus prostaglandin E2 gel for induction of labour in prelabor rupture of membranes at term and found that eventhough both the drugs are efficacious for labor induction, PGE2 gel was superior as number of doses and adverse effects like tachysystole and fetal distress are less.

Study conducted by Chaudhari et al in 2011[46]compared immediate induction with vaginal misoprostol tablets and immediate induction with vaginal dinoprostone gel in women with premature rupture of membranes at term and found that both are equally efficacious in labor induction as the induction-to-delivery interval and cesarean section rate did not differ significantly and both demonstrates a similar fetal and maternal safety profile.

Eric Frohn et al [47] compared intravaginal misoprostol 50micrograms versus 2.5mg prostaglandin E2 for cervical ripening in women with premature rupture of membranes after 34weeks of gestation in 2002. Another dose was repeated if necessary and if 6hours later, if labour has not begun yet, oxytocin treatment was started and it was found that intravaginal misoprostol was more effective that is, the induction delivery interval is less, requirement of second dose is less and also the rate of cesarean section is less but rates of tachysystole and hyperstimulation were more with intravaginal misoprostol. Neonatal outcomes were similar in both the groups.

In 2009, Monika B Nagpal et al [48] compared the safety and efficacy of oral misoprostol versus intracervical dinoprostone gel for active management of pregnancies between 37-42 weeks with PROM at term and with Bishops score of less than 5. Patients were assigned either to 4hourly application of oral misoprostol 50micrograms for a maximum of 3doses or 6th hourly intracervical PGE2 gel of 2 doses followed by oxytocin augmentation if labour has not started. Oral misoprostol is concluded to be safer and efficacious as induction delivery interval is less than intracervical PGE2 gel and also the oxytocin requirement is less and patient satisfaction was better with misoprostol group. Mode of delivery, abnormalities of uterine contractions, neonatal outcomes were comparable between two groups.

In a metaanalysis, in 2015, Zhang et al [49] evaluated the RCTs comparing the effects of misoprostol and PGE2 gel for labour induction in PROM after 34 weeks of pregnancy and concluded that misoprostol is as safe and efficacious as PGE2 gel as there is no significant difference between the two groups in induction delivery interval, rate of cesarean section and rate of neonatal intensive care unit admission. But rate of tachsystoles were significantly higher with misoprostol group.

MATERIALS AND METHODS

MATERIALS AND METHODS

1. **Study design**:

Analytical Cross - sectional Study

2. **Study duration**:

February 2021 – November 2021 (10 months)

3. **Study area**:

Department of Obstetrics and Gynaecology,

Government Raja Mirasudhar Hospital, Thanjavur.

4. **Study population**:

Term mothers with spontaneous Prelabor Rupture Of membranes (PROM) attending obstetric casualty

5. **Sampling technique**:

Multistage sampling technique

6. **Sample size**:

In a study conducted by Nivedita Jha et al [50], Comparison of efficacy and safety of sublingual misoprostol with intracervical dinoprostone gel for cervical ripening in prelabour rupture of membranes after 34 weeks of gestation,

prevalence of misoprostol usage was found to be 60%

n=4pq/d2

p=prevalence = 60%

q= 100 - p = 40%

d= allowable error = 10%

n = 4×60×40/ 10x10

n (calculated sample size) = 96

Rounding off, the final sample size (n) = 100

The 100 samples were assigned randomly into two groups which was 50 in each group

7. **Inclusion criteria**:

- Women with singleton fetus of cephalic presentation.
- Gestational age >37weeks.
- With spontaneous rupture of membranes <6hours.
- Lack of uterine contractions for atleast1hour from PROM.
- Bishops score <6 .

8. **Exclusion Criteria**:

- Women with scarred uterus.
- With any associated medical or obstetrical complications.
- With suspected cephalopelvic disproportion.
- With contraindications to vaginal delivery
- Non reassuring foetal heart rate
- Meconium staining of amniotic fluid
- Cases being referred from PHC/GH
- Women with contraindications to prostaglandins

9. **Data collection instrument**:

The schedule prepared was first prepared in English. This was then translated to local language; which was Tamil and then it was translated back by third person who was not a part of the study investigator group which was done to ensure the validity of the schedule.

The schedule was a semi structured schedule and it consisted of the initial part which had questions on basic demographic details viz., name, age, occupation, address, personal history such as alcoholism and smoking and history of past and also present medical and surgical history

The next part of the schedule consisted of questions related to current pregnancy and related events and outcome such as duration of labour, failed induction, and outcome. When the baby was delivered the information such as Appearance, Pulse rate, Grimace, Activity (muscle tone), and Respiration (APGAR) score was noted and Neonatal Intensive Care Unit (NICU) admission was also noted.

The pilot study was conducted among 10% of the samples which was approximately 10 patients, and the schedule was modified appropriately. The results which were obtained from this pilot study was not included in the final analysis.

10. Methodology:

The term mothers who came to casualty of Obstetric department, Government Raja Mirasudhar Hospital, Thanjavur, based on the inclusion and exclusion criteria, i.e., mothers who are at term (over 37 weeks of gestation) and who had spontaneous prelabour rupture of membrane (PROM) which happened less than six hours of presenting at the causality. Those in active labour are not considered for inclusion in the study. Those mothers who have been selected for the study are explained about the study procedure and written informed consent was obtained from the pregnant mother. A total of 100 mothers were selected. They were randomly assigned to either of the two groups. So that each group contains 50 term mothers with term prelabor rupture of membranes.

On enrolling in the group, the details such as name, age, previous and present obstetric history were asked for. They were also asked for any history of fever, and about surgical and medical history.

The basic anthropometric measurements such as height, weight, blood pressure, per abdominal examination were all performed to all the participants irrespective of which ever group they belonged. They were also assessed for Amniotic Fluid Index (AFI) and fetal presentation confirmed sonographically.

Temperature assessment at 4 hourly and pulse rate at every half an hour interval was measured. The biochemical investigations such as total leucocyte count and c-reactive proteins were also measured. A Swab was taken from posterior vaginal fornix of cervix of all women in the group and women were allocated randomly into one of each groups and

induced accordingly . Labour progress monitored with partograph. Induction delivery interval and the mode of delivery were noted and included in the findings of the study. All PROM mothers were started on Inj. Cefotaxim 1g iv BD immediately after admission in our institute

After the baby was born the Appearance, Pulse rate, Grimace, Activity (muscle tone), and Respiration (APGAR) score was noted down along with admission to Neonatal Intensive Care Unit (NICU). All these were measured for every mother who participated in the study irrespective of the group they were assigned.

Group A (Misoprostol group)

The mothers who were in term and with prelabor rupture of membrane, were given two doses of misoprostol (25 micrograms) four hours apart and observed for uterine contractions, fetal heart rate, cervical dilatation, mode of delivery, duration of delivery after induction and outcome and complications.

Group B (Dinoprostone gel group)

Similarly, the second group, the mothers were given a single dose of intra cervical dinoprostone gel with 0.5 milligram strength. They were also observed for uterine contractions, fetal heart rate, uterine contractions, cervical dilatation, mode of delivery, duration of delivery after induction, outcome and complications.

FLOW CHART DEPICTING THE MULTISTAGE SAMPLING TECHNIQUE

Pregnant women attending the obstetric casualty of Government Raja Mirasudhar Hospital, Thanjavur

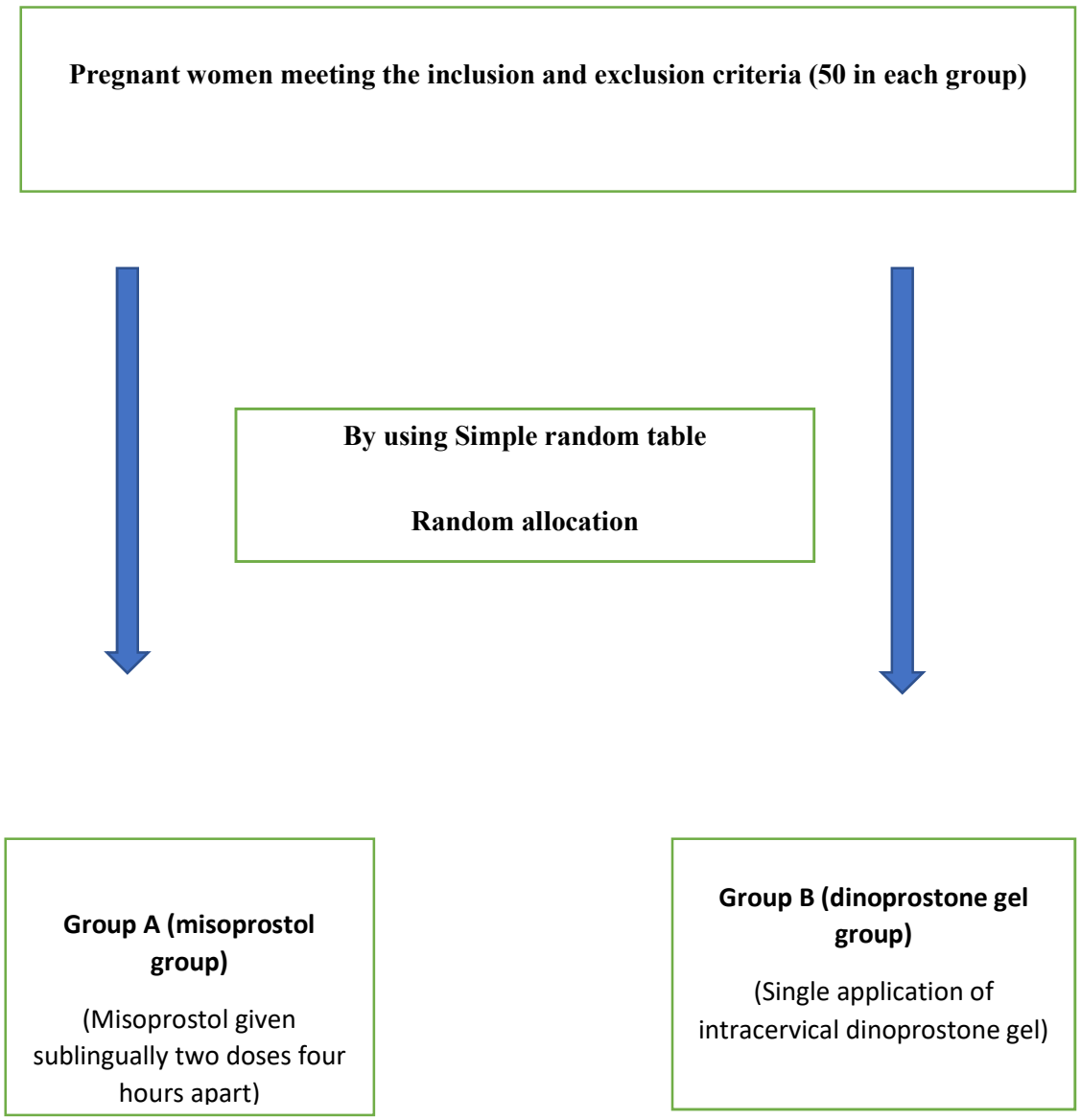
(by simple random sampling technique)

by simple random sampling technique

Among those pregnant women who were term i.e., over 37 weeks of gestation and presenting with Prelabor Rupture Of Membrane (PROM) and presenting with less than 6 hours and also with Bishops score of less than six were selected

Based on inclusion and exclusion criteria and after obtaining written informed consent the patients are included in the study and randomly assigned to either of the two groups

FLOW CHART SHOWING THE ALLOCATION OF PATIENTS INTO EACH GROUP



11. Operational definitions:

Induction of labour

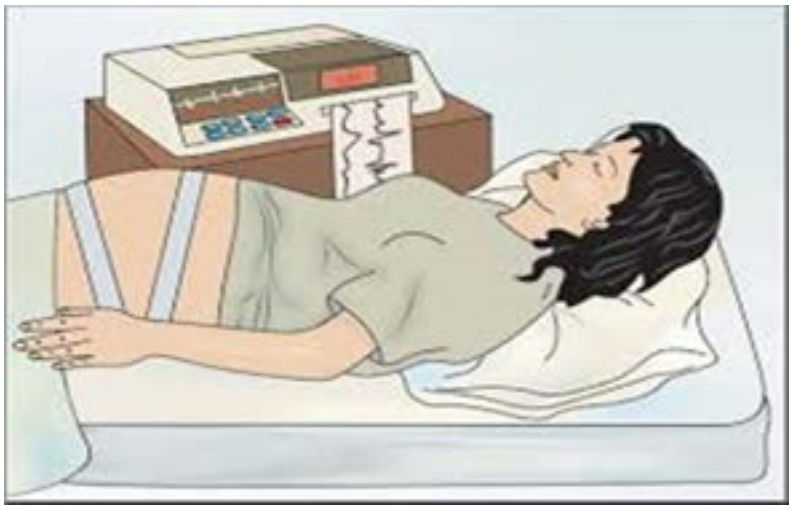
This is termed when uterine contractions are artificially initiated in a pregnant woman who is not in labour thereby helping her achieve a vaginal birth within 24-48hours [51]

Failed induction

This is defined when the uterine contractions are not regular (every 3 minutes) after one cycle of completion of cervical ripening which consists of either insertion of three intracervical PGE2 gel at 6-hourly intervals, and 12-24 hours of oxytocin administration after rupture of membranes, if feasible or one PGE2 insert (10mg) within 24hours. [51]

Non Stress test (NST)

This is done to determine the foetal heart rate and there by knowing the baby's well being. The pregnant women are made to lie in a reclining chair, and a sensor is placed around the mother's belly which measures the foetal heart rate. It is usually carried out for a period of 20 minutes. The reading suggests the well-being of the baby but cannot predict acute intrapartum obstetrical emergencies like cord prolapse



12. Ethical considerations:

The protocol which was prepared was submitted to the Institutional Ethics Committee (IEC) and permission for carrying out the study was obtained before the study was started. The pregnant mothers were interviewed in person and various anthropometric measurements and blood for biochemical markers, swab for vaginal microflora was drawn after obtaining informed written consent. The privacy and confidentiality of the mother was conserved

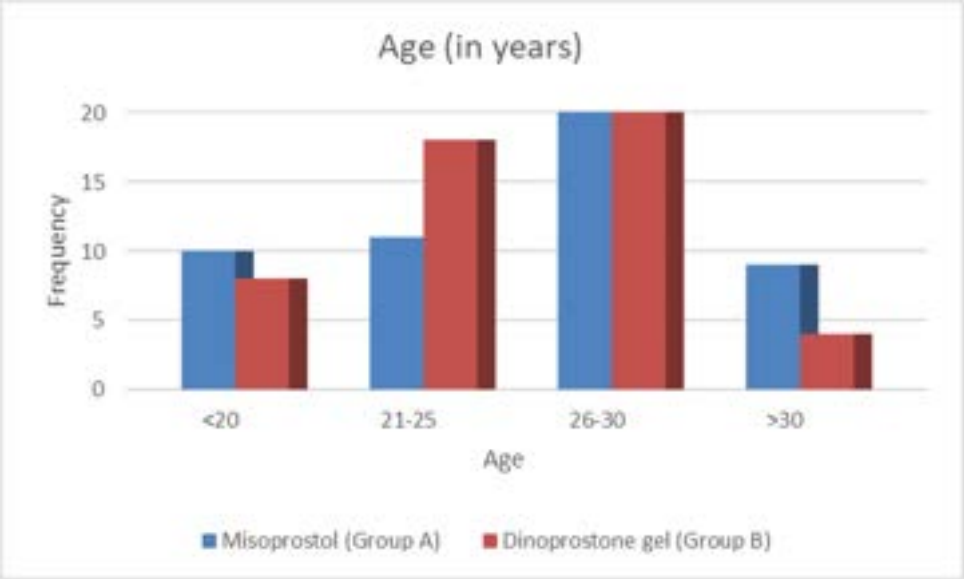
13. **Statistical Analysis:**

Data was collected in the schedule and responses were entered in the Microsoft excel. Using Epi info free software available online, the descriptive statistics such as frequency and percentages were calculated. The association between descriptive variables was found using chi square test. The difference and similarity between the groups were analysed using repeated measures ANOVA and inferential statistics student t test and paired t test were done to find out the significant difference between means of two groups. The value less than or equal to 0.05 was inferred statistically significance.

OBSERVATION AND RESULTS

RESULTS

Fig 1: Age distribution of the study participants



In this study, the median age of the study participants was 25 years (± 8.48) in group A and it was 26.2 (± 6.42). About 10 in group A and 8 in group B belonged to age less than 20 years. About 11 of them belonged to 20 -25 years of age in group A and 18 in group B, followed by 26-30 years, 20 in group A and 20 in group B. 09 participants in group A and 04 in group B belonged to age over 30 years category. The percentage of age distribution in both groups is shown in fig1

Table . 1: Difference of means of age between the groups

Age	N	Mean	SD	ANOVA	p value
Group A (sublingual misoprostol)	50	25.0	8.48	6.03	**0. 016***
Group B (intracervical dinoprostone gel	50	26.2	6.42		

In the above table.1, the difference between the means of age among the group A and group B was found to be 6.03 with a p value of 0.016 which was statistically significant.

Fig 2 :Height of the study participants

Among the study participants, over 170 centimeters were 07 in group A and 04 in group B, while 06 in group A and about 09 in group B were less than 150 centimeters. About 25 in group A and about 22 in group B were belonging to 151-160 centimeters. Rest 12 in group A and 15 in group B were belonging to 161-170 centimeters. The height of the study participants as shown in fig 2.

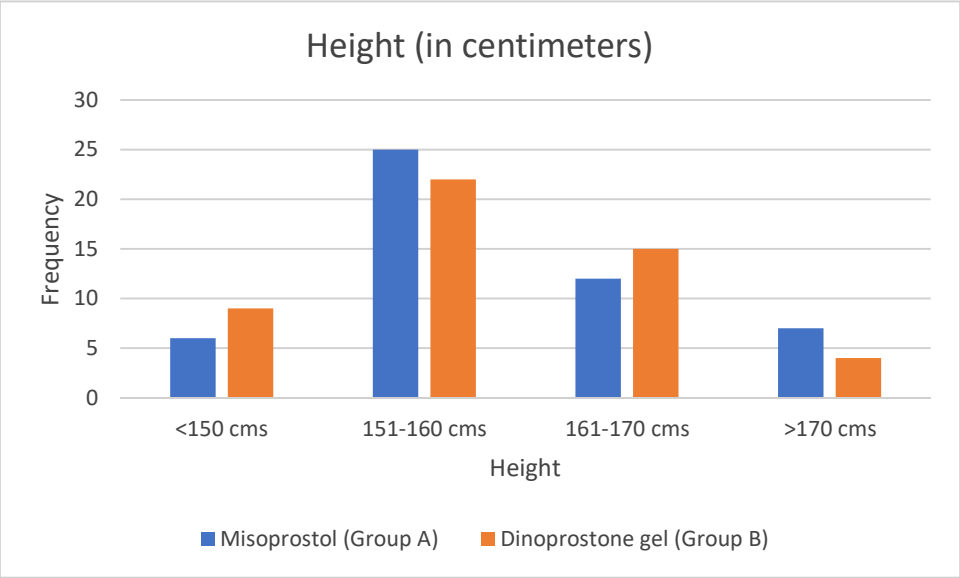
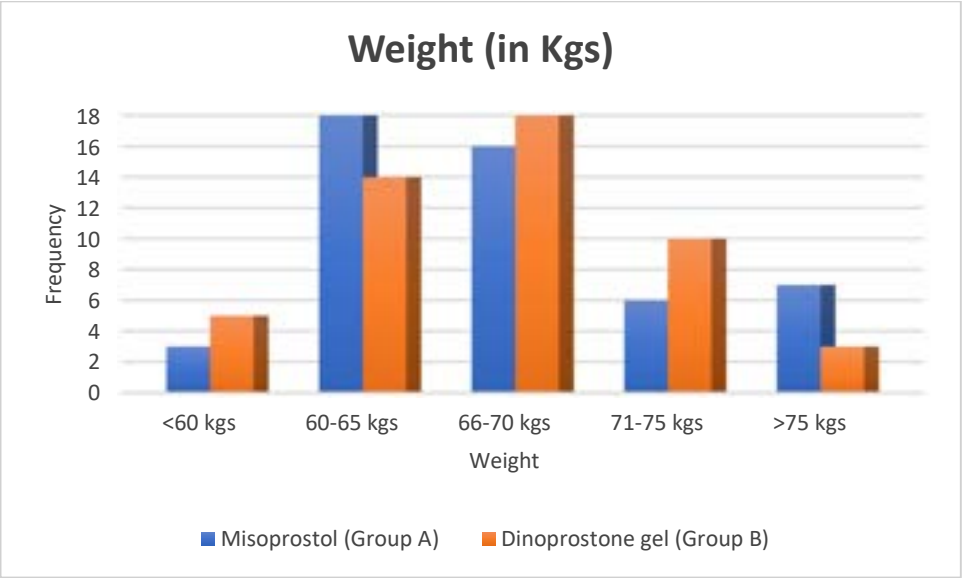


Table 2. : Correlation of Distribution of height to delivery outcome

Parameter	Group	N	Mean	Std. deviation	t test
Height	A (with misoprostol)	50	160.01	4.10	0.51
	B (with dinoprostone gel)	50	159.70	4.67	

From the above table 2., the average height of the participants in the intervention group is 160 centimetres and that of the control group is 159.7.7 centimetres. t value is 0.51 which is very much small and insignificant

Fig 3 : Weight of the study participants



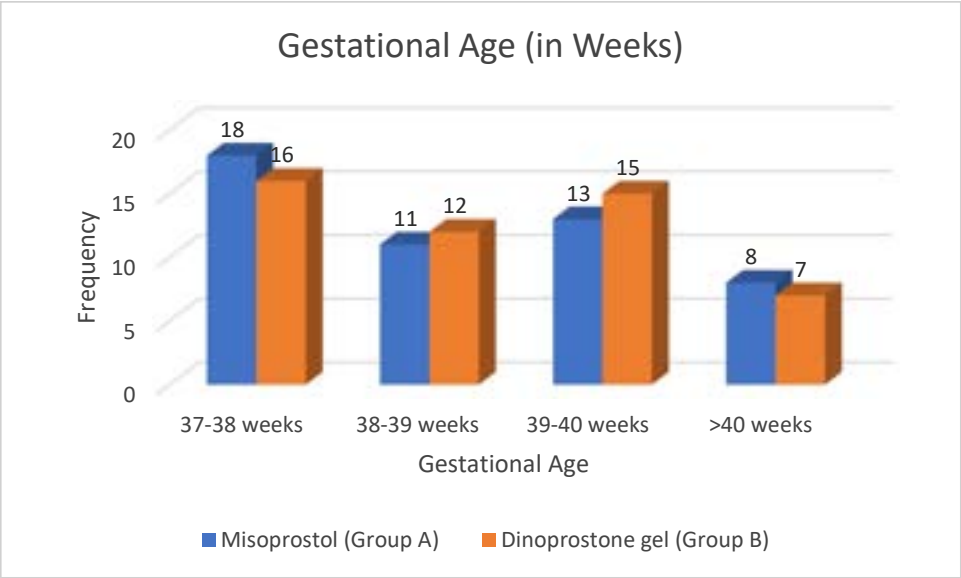
Among the study participants only 3 of the participants in group A and 5 in group B had weight less than 60 kilograms, 18 of the participants in group A and 14 of the participants in group had weight between 60-65 kilograms, 16 of the participants in group A and 18 in group B had weight between 66-70 kilograms, 6 of the participants in group A and 10 in group had weight between 71-75 kilograms and 7 of the participants in group A and 3 in group B had weight over 75 kilograms. The weight of the study participants as shown in fig 3

Table 3 : Correlation of Distribution of weight to delivery outcome

Parameter	Group	N	Mean	Std. deviation	t test
Weight	A (with misoprostol)	50	60.41	4.68	0.81
	B (with dinoprostone gel)	50	61.96	4.01	

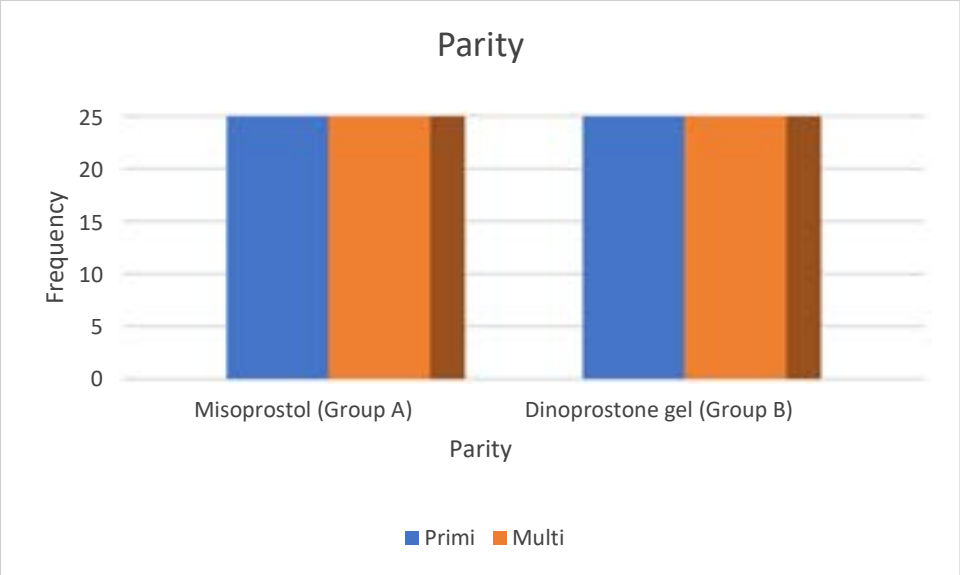
In the above table 3., The weight between the two groups mean is 60.41 in case group and 61.9 in control group and the t value is insignificant with a value of 0.187

Fig 4: Gestational Age distribution of the study participants:



In our study the gestational age distribution of the participants were about 18 belonged to Group A and 16 belonged to group B of them were 37-38 weeks of gestational age, 11 belonged to group A and 12 belonged to 38-39 weeks were of gestational age, about 13 belonged to Group A and 15 belonged to Group B of them were 38-39 weeks were of gestational age. And about 8 belonged to Group A and 7 belonged to Group B of them were over 40 weeks of gestational age. The frequency of age distribution is shown in fig 4

Fig 5: Parity in the study population



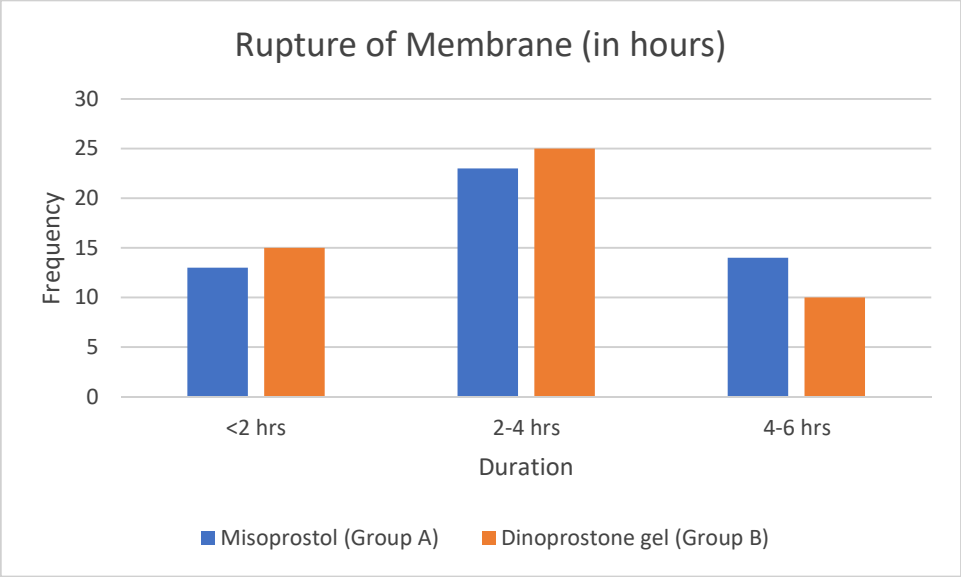
In this study, half of the study participants in both group A (25) and group B (25) were primi. Then the rest in group A (25) and Group B (25) were multigravida. This is shown in figure 5

Table 4 : Distribution and Association of Parity to mode of induction

Parity	Mode of induction		$X2$	p value
	With misoprostol (Group A)	With dinoprostone gel (Group B)		
Primi	25	25	4.612	0.12
Multi	25	25		
Total	50	50		

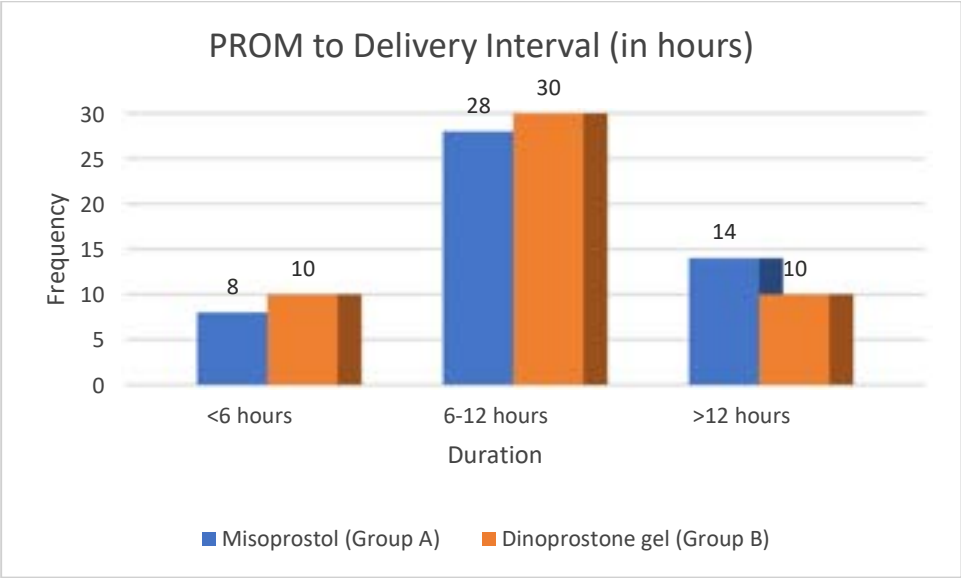
In the above table 4., In Primi gravida (n=25) in group A i.e those induced with misoprostol and in those induced by using dinoprostone gel i.e Group B were also primi gravida (n= 25). In group A about 25 were multi gravida in group A and in group B (n=25) were multi gravida. The chi square value (X^2) was 4.612 and p value was 0.12 which was statistically insignificant.

Fig 6: Time since rupture of Membrane distribution of the study participants:



In our study, 13 of the women from group A and 15 of the women in group B presented to the hospital within 2 hours of rupture of membrane. About 23 of the women from group A and 25 of the women in group B presented to the hospital within 2-4 hours of rupture of membrane and 14 of the women from group A and 10 of the women in group B presented to the hospital within 4-6 hours of rupture of membrane. The frequency of time of rupture of membrane distribution is shown in fig 6.

Fig 7: PROM to delivery interval in the study population



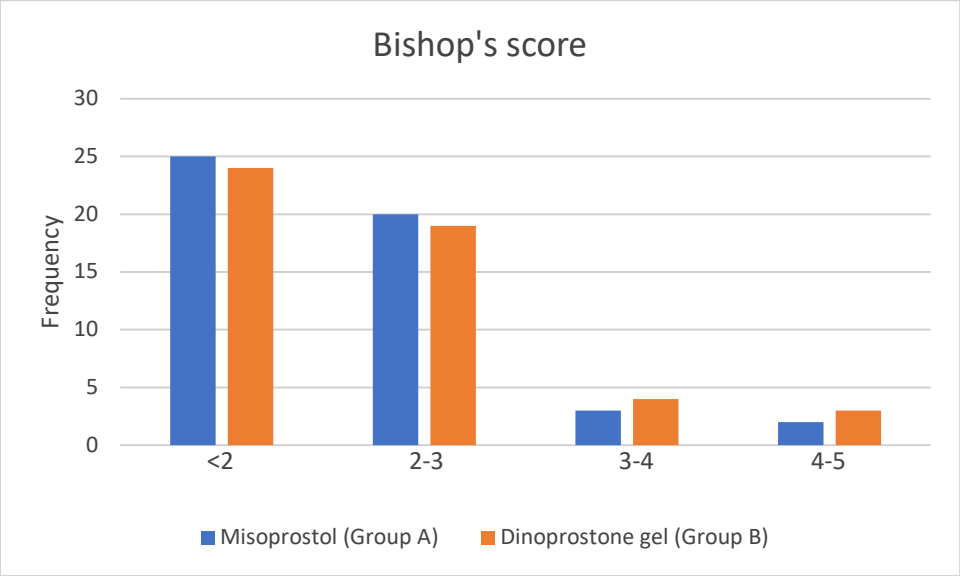
In this study, the study participants in group A (8) and group B (10) had PROM to delivery interval less than 6 hours. Then 28 participants in group A and 30 in group B had PROM to delivery interval 6-12 hours. The rest of study participants in group A (14) and group B (10) had PROM to delivery interval over 12 hours. This is shown in fig 7.

Table 5 : Correlation between PROM and delivery interval

PROM to delivery Interval (in hours)	Mode of induction	N	Mean	Std. Deviation (±)	ANOVA	p value
< 6 hours	Group A (with misoprostol)	10	4.54	2.11	2.672	**0.053***
	Group B (with dinoprostone gel)	8				
6-12 hours	Group A (with misoprostol)	30	8.12	3.14	1.567	0.132
	Group B (with dinoprostone gel)	20				
>12 hours	Group A (with misoprostol)	10	11.52	3.42	1.823	0.141
	Group B (with dinoprostone gel)	22				

In the above table., correlation between PROM and delivery interval is found to be statistically significant only at less than 6 hours with a p value of 0.053 and all the other intervals they are not significant.

Fig 8 : Bishops Score of the study participants



Among the study participants, 2 of them in group A and 3 persons in group B had bishops score of 4-5, 3 of them in group A and 4 persons in group B had bishops score of 3-4, 20 in group A and 19 persons in group B had bishops score of 2-3, 25 in group A and 24 persons in group B had bishops score of less than 2. Bishops score less than 6 of study participants as shown in fig 8.

Table 6 : Distribution and Association of Bishops score among the study participants

Bishops Score (time interval in hours)	Mode of induction	N	Mean	Std. Deviation (±)	ANOVA	p value
At 0 hours	Group A (with misoprostol)	50	2.52	0.53	32.51	**0.00***
	Group B (with dinoprostone gel)	50	2.61	0.56		
At 4 hours	Group A (with misoprostol)	50	3.61	0.61	7.19	**0.01***
	Group B (with dinoprostone gel)	50	3.54	0.58		
At 6 hours	Group A (with misoprostol)	50	3.82	0.68	2.20	0.12
	Group B (with dinoprostone gel)	50	3.65	0.61		

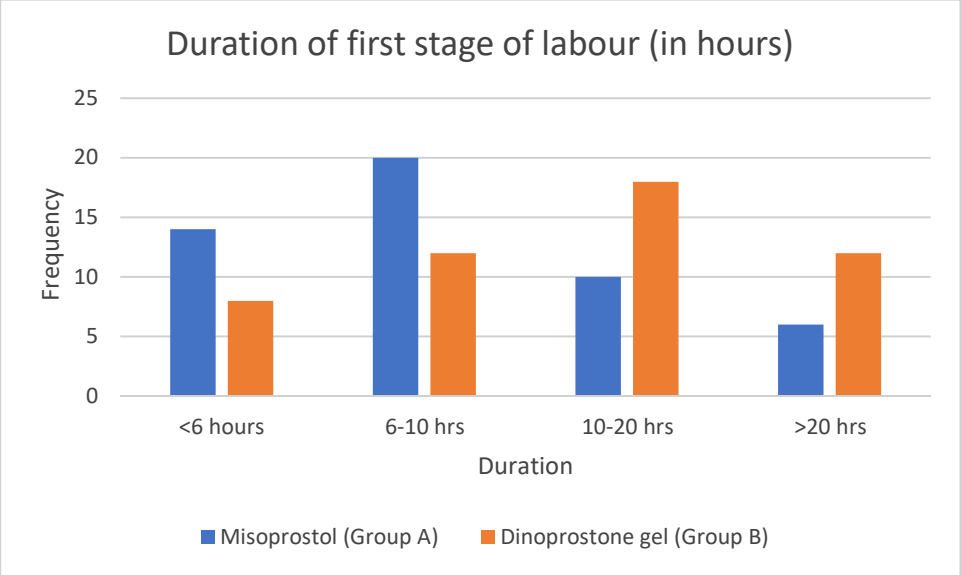
In the above table 5., Bishop score at '0' hour was similar in both the groups. In Group A the one in which misoprostol is used for induction of labor the Bishop score at '0' hour was 2.52, in dinoprostone gel group B, the Bishop score at '0' hour was 2.61

In Group A the one in which misoprostol is used for induction of labor the Bishop score at 4 hour was 3.61, in dinoprostone gel group B, the Bishop score at 4 hour was 3.54

In Group A the one in which misoprostol is used for induction of labor the Bishop score at 6 hours was 3.82, in dinoprostone gel group B, the Bishop score at 6 hours was 3.65.

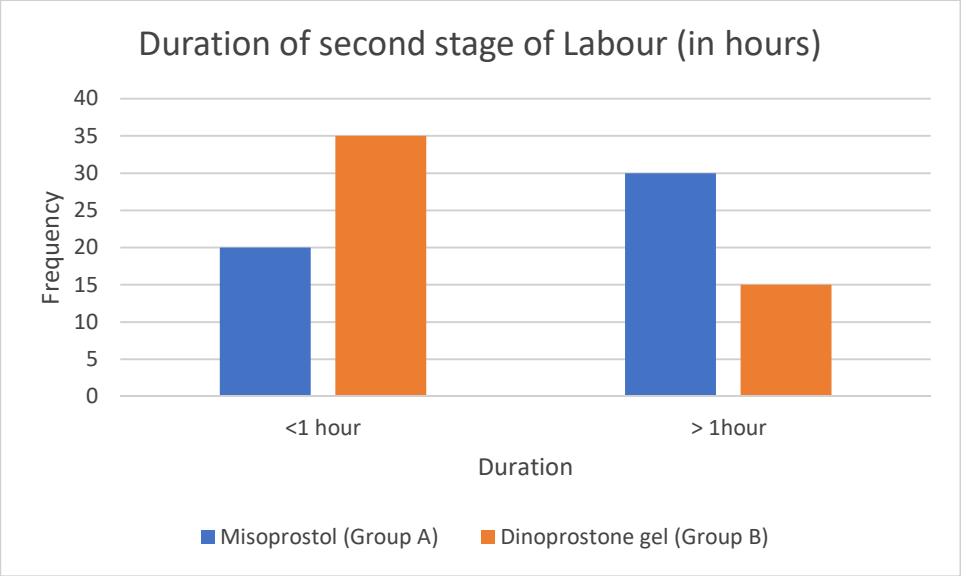
The ANOVA value at 0 hours was found to be 32.51 and p value was found to be 0.00 which was statistically significant. And at 4 hours the ANOVA value was 7.19 with p value of 0.01which was also statistically significant. At 6 hours was found to be 2.20 and p value was found to be 0.12 which was statistically insignificant

Fig 9: Duration of labour (first stage) in the study participants



In this study , 14 women from group A and 8 from group B had duration of < 6 hours. **20 women from group A and 12 women from group B had 6-10 hours of first stage duration. 10 women from group A and 18 from group B had 10 - 20 hours of first stage duration and only 6** from group A and 12 from group B had delivery interval over 20 hours.

Fig 10 : Duration of labour(Second stage) in the study participants



In this study about 30 women from group A and 15 from group B had their baby delivered within 1 hour second stage of labour. 20 women from group A and 35 women from group B had their baby delivered over 1 hour. This is shown in Fig 10.

Table 7 : Correlation between first stage of labour and the groups

First stage of labour (interval in hours)	Mode of Induction	N	Mean	ANOVA	p value
<6	Group A (with misoprostol)	14	4.86	2.981	**0.052***
	Group B (with dinoprostone gel)	8			
6-10	Group A (with misoprostol)	20	8.54	1.921	0.731
	Group B (with dinoprostone gel)	12			
10-20	Group A (with misoprostol)	10	12.42	2.895	0.062
	Group B (with dinoprostone gel)	18			
>20	Group A (with misoprostol)	6	21.25	1.723	0.091
	Group B (with dinoprostone gel)	12			

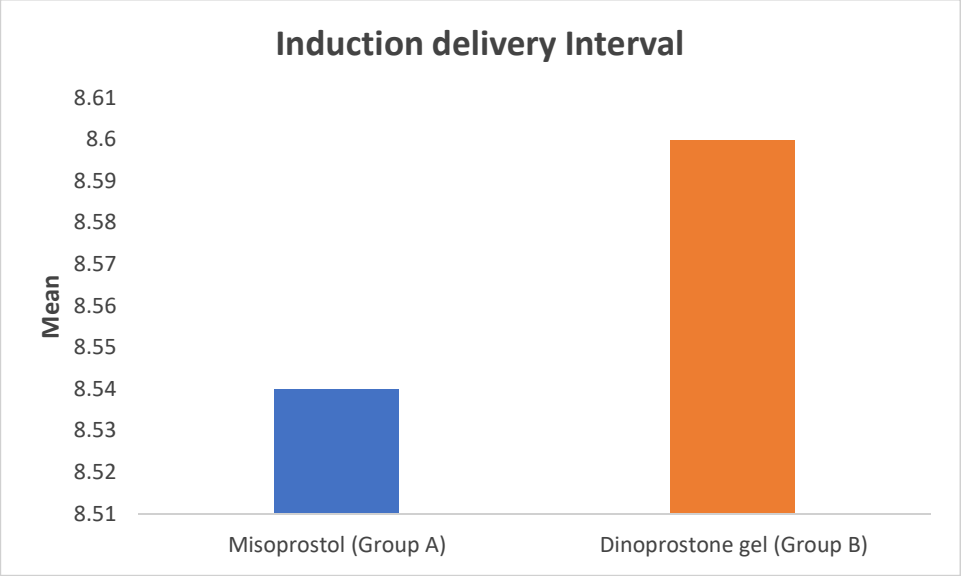
In the above table, only at time interval less than 6 hours is found to be statistically significant with a p value of 0.052 with the drugs used for induction i.e, among the groups

Table 8 : Correlation between second stage of labour and the groups

second stage of labour (interval in hours)	Mode of Induction	N	Mean	ANOVA	p value
<1	Group A (with misoprostol)	10	4.21	4.326	**0.021***
	Group B (with dinoprostone gel)	12			
>1	Group A (with misoprostol)	18	8.65	0.061	1.221
	Group B (with dinoprostone gel)	20			

In the above table, only at time interval less than 1 hour was only found to be statistically significant with a p value of 0.021 with the drugs used for induction i.e, among the groups

Fig 11: Mean induction delivery interval measured in the study population



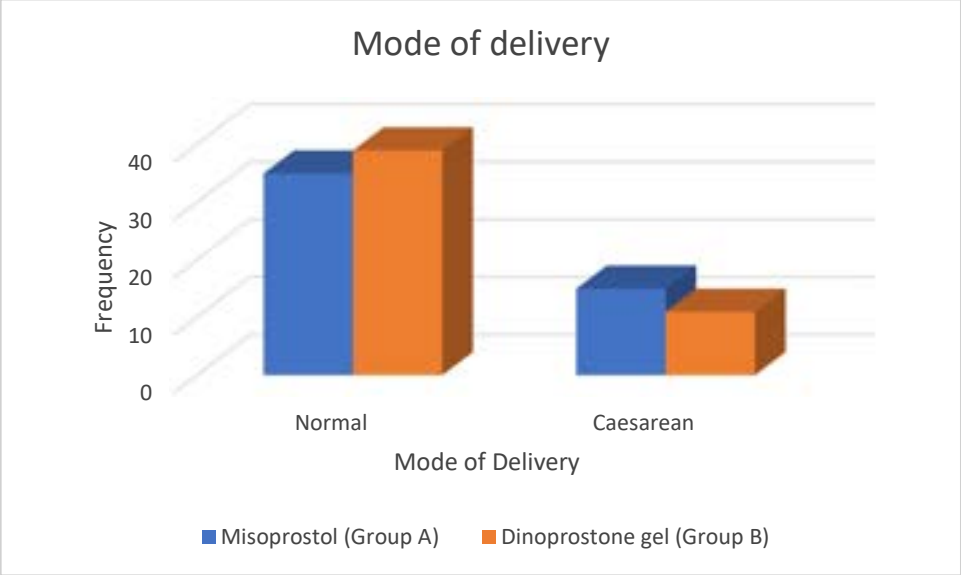
In the shown figure10, the mean induction time in misoprostol group (Group A) was found to be 8.54 and in group B who were given dinoprostone gel was found to be 8.60 hours.

Table 9 : Distribution and Association of Delivery interval among the study participants

Mode of Induction	N	Induction Delivery Interval Mean	Std. Deviation (±)	ANOVA	p value
Group A (with misoprostol)	50	8.54	1.21	132.90	**0.001***
Group B (with dinoprostone gel)	50	8.60	1.34		
Total	100	8.57	1.27		

In the above table 6. The induction delivery interval was almost equal in both the groups i.e. group A with Misoprostol which was 8.54 hours and in the Group B which got dinoprostone gel for induction was 8.60 hours. The ANOVA test and the difference of the means of these two groups was found to be statistically significant (p <0. 001)

Fig 12 : Mode of Delivery in the study participants



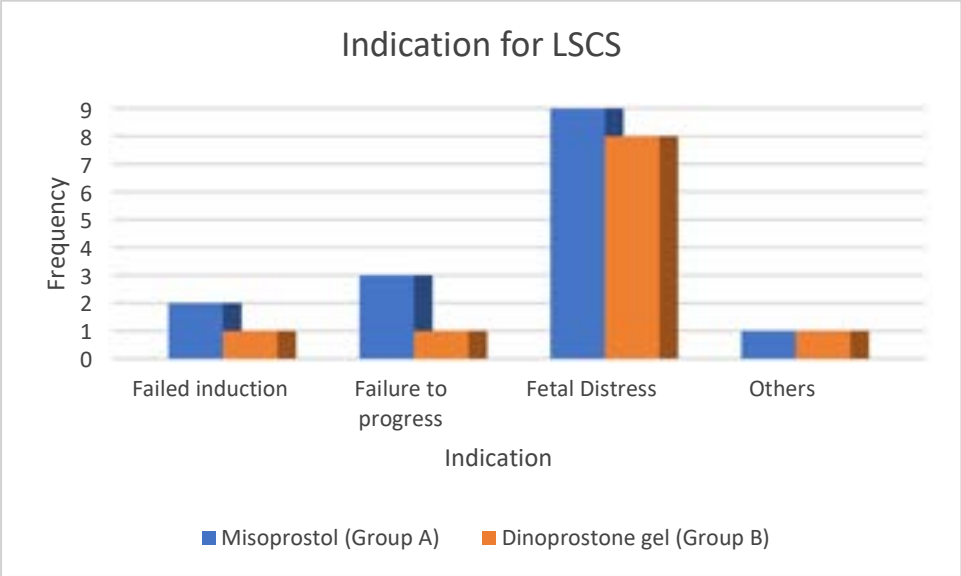
Among the study participants 35 of the women belonging to Group A and 39 belonging to group B had delivered vaginally. The rest 15 belonging to Group A and 11 belonging to group B had delivered by Caesarean delivery. This is shown in Fig.12

Table. 10: Association between mode of delivery and induction

Mode of delivery	**Mode of induction**		**N**	***X*2**	**P value**
	Group A (with misoprostol)	Group B (with dinoprostone gel)			
Normal	35	39	74	5.82	**0.048***
Caesarean	15	11	26		
Total	50	50	100		

In the above table.7, Mode of delivery was compared in two groups labour natural was found in 35 of them in group A who had misoprostol, and 39 had normal labour in group B with dinoprostone gel. Caesarean was found in 15 of them in group A who had misoprostol, and 11 had Caesarean in group B with dinoprostone gel. By using ANOVA test and the difference of the means of these two groups was found to be statistically significant (p = 0.048).

Figure 13: Indications for LSCS among the study participants



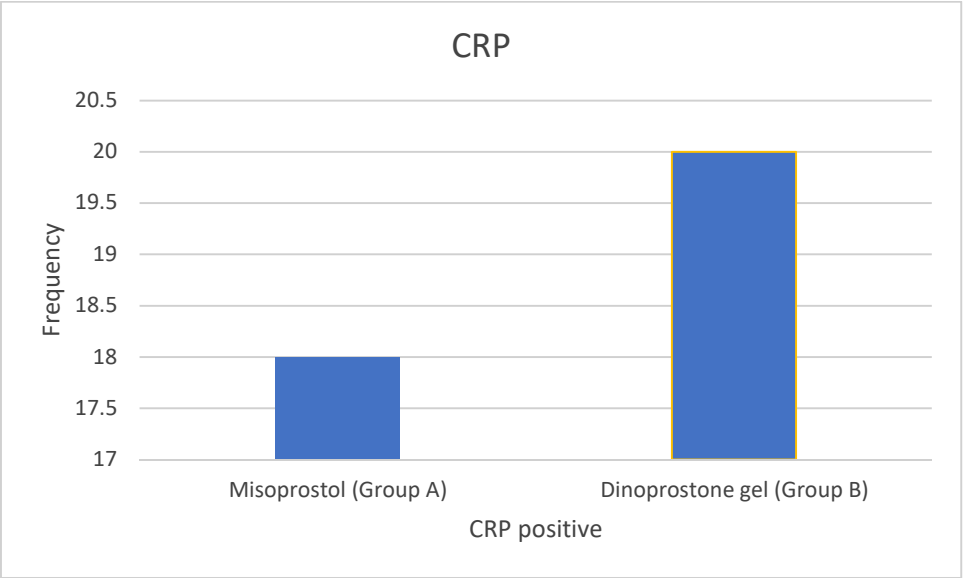
In the study, about 2 participants in group A and 1 in group B had failed induction to be the reason for LSCS. about 3 participants in group A and 1 in group B had failure to progress be the reason for LSCS. 9 participants in group A and 8 in group B had fetal distress to be the reason for LSCS. And 1 participant each in group A and 1 in group B had other reason for LSCS. This is shown in fig 13.

Table 11 : Association between indication for LSCS and mode of induction

Group A (with misoprostol)		Group B (with dinoprostone gel)	$X2$	p value
Failed induction	2	1	5.621	**0.045***
Failure to progress	3	1	7.789	0.651
Fetal Distress	9	8	9.265	**0.011***
Others	1	1	4.652	0.084

In the above table , the association between Indication for LSCS and the groups, failed induction was found to be statistically significant with a chi square value of 5.621 (p = 0.045) and the indication fetal distress was found to be statistically significant with a chi square value of 9.265 (p = 0.011) rest all were not statistically significant.

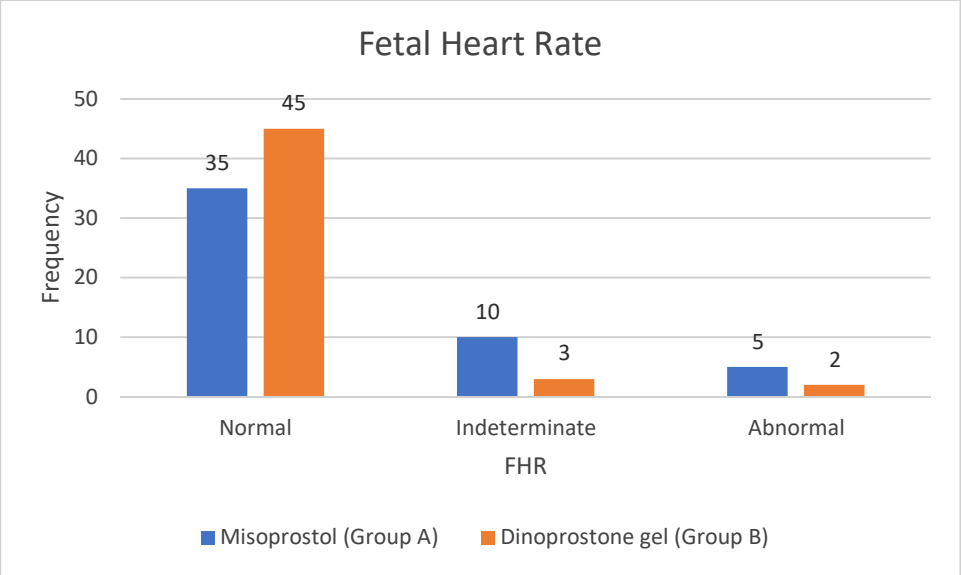
Fig 14: C reactive protein marker in the study population



In our study the pregnant mothers who presented with term rupture of membrane and who had reactive C protein titres positive in group A were 18 of them and in group B was 20 of them the rest of the participants in both the groups tested negative for C Reactive Protein. This is shown in Fig. 5.14

In this study most participants had normal leucocyte count, in group A (98%) and Group B (99%) and the rest group A (2%) and Group B (1%) had mildly elevated total leucocyte count.

Fig 15 : Fetal Heart Rate (FHR) observed among study participants



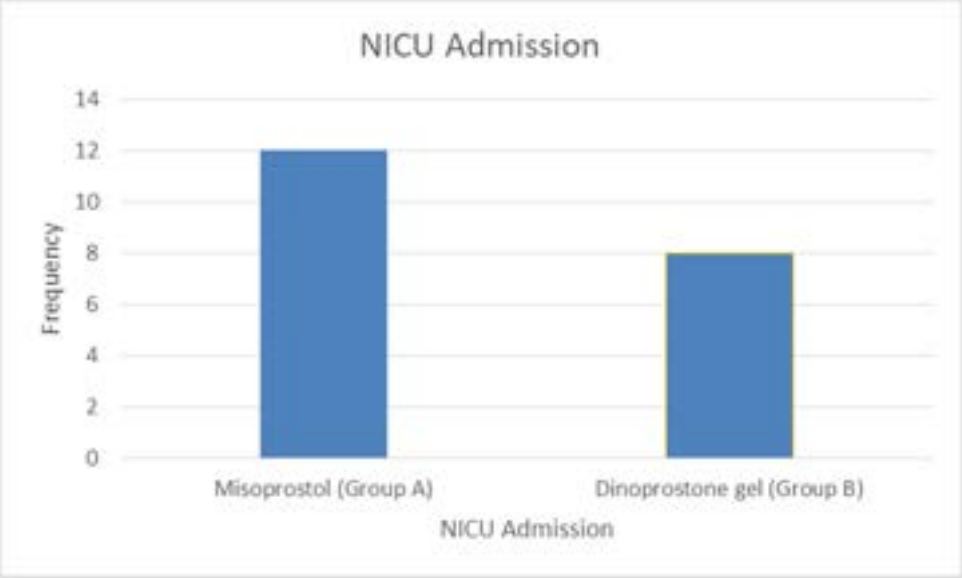
Among the study participants , 35 babies in group A and 45 in group B had normal heart rate. 10 babies in group A and 3 babies in group B had indeterminate heart rate and 5 babies in group A and 2 in group B had abnormal heart rate This is shown in Fig. 15

Table 12: Association between fetal Heart rate and mode of induction

Fetal Heart Rate		**Group A (with misoprostol)**	**Group B (with dinoprostone gel)**	***X*2**	**p value**
Normal		35	45	6.854	**0.022***
Indeterminate		10	3	8.576	0.782
Abnormal		5	2	9.281	**0.013***

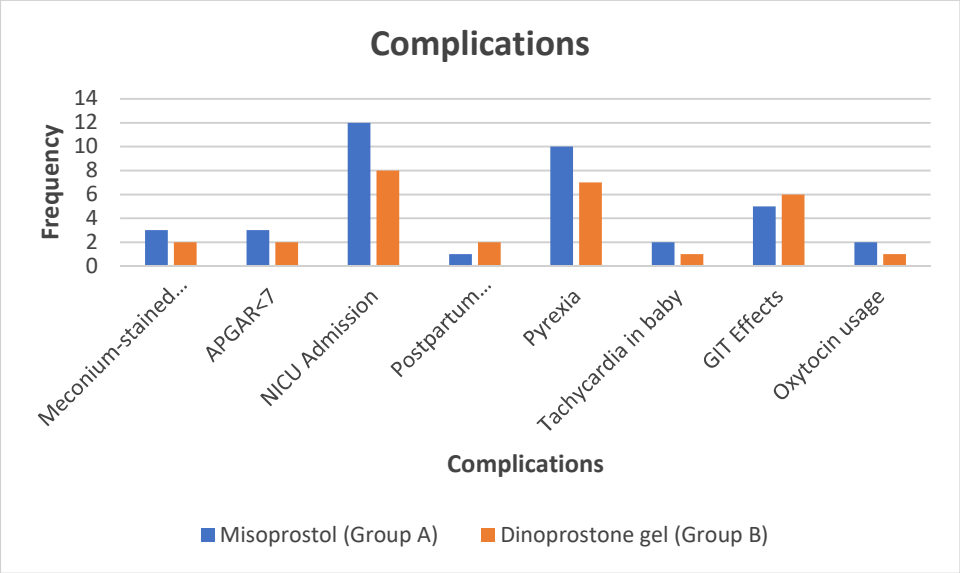
In the above table , the association between Fetal heart rate and the groups, Normal was found to be statistically significant with a chi square value of 6.854 (p = 0.022) and Abnormal heart rate was found to be statistically significant with a chi square value of 9.281 (p = 0.013) rest all were not statistically significant.

Fig 16 : Neonates needing intensive care unit admission of the study participants



In our study, about 12 babies out of 50 babies born to mothers who had misoprostol for induction i.e. in group A required NICU admission. About 8 babies out of 50 babies born to mothers who had dinoprostone gel for induction i.e. in group B required NICU The rest 70% did not require admission in Neonatal Intensive Care Unit (NICU) This is shown in Fig. 16

Fig 17: Complications observed in the study population



The above Figure 17, shows the frequency of complication observed in group A (induction with misoprostol) and group B (induction with dinoprostone gel). When observed the overall complications was less in Group B than in group A.

Table 13 : Association between mode of induction and Complications

Complications observed		Mode of induction		X^2	p value
		Group A (with misoprostol)	Group B (with dinoprostone gel)		
Meconium-stained Amniotic Fluid	Yes	03	02	6.635	**0.001***
	No	47	48		
APGAR<7	Yes	03	02	2.705	0.065
	No	47	48		
NICU Admission	Yes	12	08	5.023	**0.031***
	No	38	42		
Postpartum Hemorrhage	Yes	01	02	0.151	1.312
	No	49	48		
Pyrexia	Yes	10	07	7.362	**0.042***
	No	40	43		
Tachycardia in baby	Yes	02	01	7.328	**0.041***
	No	48	49		
GIT Effects	Yes	05	06	0.125	1.452
	No	45	44		
Oxytocin usage	Yes	01	02	0.326	0.621
	No	49	48		

In the above table 13., Meconium-stained Amniotic Fluid, 3 of the participants were found to be from group A and 2 were from group B. The babies born 12 from group A were requiring NICU admission and in group B only 8 babies required NICU admission. Pyrexia complaint was observed in 10 participants in group A and 7 in group B. when X^2 was done for finding out the association, Meconium-stained Amniotic Fluid with X^2 value of 6.635 and p value of 0.001 which was statistically significant. The same like was observed in NICU admission (p = 0.031), pyrexia and induction (p = 0.042) and also tachycardia in baby (p =0.041) was also statically significant.

DISCUSSION

DISCUSSION

The study which was conducted at Government Raja Mirasudhar Hospital, Thanjavur as a **Comparative study of cervical ripening with sublingual misoprostol and intracervical dinoprostone gel in term pre labour rupture of membranes** over a period of 10 months. 100 women who were fitting our inclusion criteria were randomized to either sublingual Misoprostol or intracervical dinoprostone gel in a way that each group had 50 participants each.

In this study patients with term rupture of membranes who came to the hospital were given either sublingual misoprostol or intracervical dinoprostone gel to groups assigned randomly. The indication for induction according to this study was for those presenting to obstetric casuality within 6 hours of rupture of membrane and not having uterine contractions for almost 1hour after rupture of membranes and with unfavourable cervix of Bishops score <6 at the time of admission.

INDUCTION TO DELIVERY INTERVAL

In this study, the mean induction delivery interval observed in group A was 8.54 hours and in group B was 8.60 hours. The result was analyzed using ANOVA and the difference of means of the two groups was found to be statistically significant with a p value 0. 001 , that is , according to this study, induction with sublingual misoprostol results in a quicker delivery than induction with intracervical dinoprostone gel which is the same as in other studies.

Induction-delivery interval	Group A	Group B
Nivedita Jha et al(2015) [50]	8.3+_3.6hrs	12.2+_6.6hrs
Walid Denguezli et al(2007) [51]	14.9 hrs(vaginal misoprostol)	15.8 hrs
Veena B et al (2016) [52]	35.8% delivered within 12hours	26% delivered within 12hours
N S Chitrakar et al (2012) [53]	3.91hrs (25mcg intravaginal)	5.72hrs
Sachin Wankhede [37](2017)	22.36hrs (expectant)	15.5hrs
My study	8.54hrs	8.6hrs

PROM TO DELIVERY INTERVAL

In the present study, those who delivered within 6hours are 8% on group A, 10% on group B.28% on groupA and 30% on groupB delivered within 6-12 hours of rupture of membranes and 14% in group A and 10% in groupB delivered more than 12 hours of membrane rupture. As all the women included in the study were induced, PROM-delivery interval was less than in other studies.

	PROM to delivery interval	Limitations
Dr.Abirami et al(2021)[32]	<12hours- 10% 12-24hrs- 59%% >24hrs- 31%	It is a retrospective, non comparative, observational study and mothers were not induced
Sachin W et al(2017)	22.36 hours for expectant group 15.5 hours for induction with intracervical PGE2	Prospective study where mothers are divided into expectant management in one group & intracervical PGE2 induction in other group.
Sailaja et al (2017)	Mean duration of 20.2hours	A prospective cross sectional study where labor was induced based on Bishops score with prostaglandins
CH B Sridevi et al (2020)	Majority delivered in 13-24 hours of PROM.	Prospective study where maternal and fetal outcomes are studied. Ni induction done.
Anjali Gupta et al (2018)	23.34 hour with expectant management	17.212 hour
My study	Majority induced delivered in 6-12 hours	

MODE OF DELIVERY

In our study, about 35 (70%) participants in group A and 38 (76%) in group B had normal delivery. And 15 (30%) in group A and 12 (24%) in group B were put in for caesarean delivery. When analyzed chi square value was found to be 5.911 with a p value of 0.05, which was statistically significant. And from all the available studies comparing expectant management versus any method of induction in PROM, rate of vaginal delivery is high. This shows that only a small proportion of PROM mothers will go for LSCS. In this present study also, majority delivered vaginally.

	Group A	Group B
Veena B et al (2016)	15.8% LSCS	32.6% LSCS
Anjali Gupta et al (2018)	2%(expectant group) LSCS	16% LSCS
Sailaja et al, 2017	Vaginal delivery in 70%, Instrumental delivery in 2.5% 27.5% had LSCS	
Dr. Abirami et al, 2021	50.81% delivered vaginally 49.19% delivered via LSCS	Statistically not significant. Higher incidence of LSCS related to high rates of induction and maternal co-morbidities
My study	30% LSCS	24% LSCS

WOMEN ENTERED INTO ACTIVE LABOUR

In this study, At 4 hours after induction mean Bishop's score in group A is 3.61 whereas in group B is 3.54 which is statistically significant. This indirectly shows that more number of women induced with misoprostol has progressed well into active phase of labour.

DURATION OF FIRST STAGE OF LABOUR

In this study 20% of women in group A had duration of 6 to 19 hours whereas 18% of women in group B had duration of 10 to 20 hours. but these differences are not stastically significant. In the present study 14% in group A had duration of 1st stage <6 hours whereas in group B it is 8% which is only statstically significant and it implies that among people induced with misoprostol more people had duration of 1st stage < 6 hours than those induced with intracervical dinoprostone gel.

DURATION OF SECOND STAGE OF LABOUR

In this study, 12% in group B and 10% in group A had duration of 2nd stage < 1hour which is statistically significant implying that dinoprostone gel had shorter 2nd stage of labour.

FAILED INDUCTION

In this study, 2 in group A and 1 in group B has failed induction which is statistically significant implying that failed induction with misoprostol was more.

INDICATION FOR LSCS

The most common indication for LSCS in this study is fetal distress. 9 in group A ,8 in group B had been taken for LSCS in view of fetal distress. This shows that sublingual misoprostol has got more rate of fetal distress. Failed induction in group A is 2 whereas in group B it is 1 and this difference is statistically significant in this study implying that sublingual misoprostol has got more failed induction than intracervical dinoprostone.

	Most common indication for LSCS
CH B Sridevi et al(2020)	Non reassuring fetal status(29.6%)
Dr. Abirami et al(2020)	Fetal distress(25.6%)
Sailaja et al(2017)	Failure to progress(45.45%)
My study	Fetal distress(65.4%)

AGE DISTRIBUTION

In the present study, majority of cases are in 26-30years of age and the median age of the participants were 25 years with a deviation of ± 8.48 years in the group A where they were induced with sublingual misoprostol but in group B who were induced with intracervical dinoprostone gel the median age was found to be 26.2 years with a standard deviation of ± 6.42. In our study the difference of means of the two groups was found to be 6.03 and p value of 0.016 which was statistically significant. Though in a study conducted by Shruti Gupta et al in 2019 and another study by Sailaja et al in 2017 , the most common age group was 20-24 years.

	<20 yrs	21-25	26-30	>30
Bhupesh et al (2016) [54]	13%	64%	17%	6%
My study	18%	29%	40%	13%

COMPLICATIONS OF INDUCTION:

MATERNAL COMPLICATIONS:

Pyrexia

In the study, 10 (20%) participants who were induced by misoprostol sublingually (Group A) and 7 (14%) among those who were induced by dinoprostone gel (Group B) had pyrexia with a chi square value of 7.362 and a p value of 0.042 which was statistically significant. Hence maternal pyrexia is more common with misoprostol in this study.

GIT Effect*s*

In this study only 5 (10%) participants who were induced by misoprostol sublingually (Group A) and 6 (12%) among those who were induced by dinoprostone gel (Group B) had GIT effect with a chi square value of 0.125 and a p value of 1.45 which was statistically significant. According to this study, GIT effects like diarrhea are more common with dinoprostone gel.

Postpartum hemorrhage

In our study only 1 participant who were induced by misoprostol sublingually and 2 among those who were induced by dinoprostone gel had PPH. the chi square when calculated the value obtained was 0.151 and p value was 1.312 which was statistically insignificant. In this study misoprostol is having higher rates of postpartum hemorrhage than dinoprostone. All cases of postpartum hemorrhage were managed medically.

Nil other significant maternal morbiditiy observed in the study group.

Fetal complications:

Meconium-stained amniotic fluid

In our study 3 participants who were induced by misoprostol sublingually (Group A) and 2 among those who were induced by dinoprostone gel (Group B) had meconium-stained fluid with a chi square value of 6.635 and a p value of 0.001 which was statistically significant and it was concluded that misoprostol induction is associated more with meconium stained amniotic fluid.

NICU admission

In this study only 12 (24%) among the babies born to mothers who were induced by misoprostol sublingually (Group A) and 8 (16%) among the babies born to mothers who were induced by dinoprostone gel (Group B) had to be admitted in NICU**,** with a chi square value of 5.023 and a p value of 0.031 which was statistically significant.

	Maternal morbidity	Fetal morbidity
Sailaja et al(2017)	17.5% with febrile morbidity being the most common	26% birth asphyxia - most common
Arpita et al(2017)	26% - chorioamnionitis	30% - early on set neonatal sepsis
Shruthi guptha et al(2019) [33]		26% - NICU admission
Tigist endale et al(2016) [35]	22% - puerperal sepsis	33.5%

SUMMARY

SUMMARY

1. The maximum age group in the study was between 26-30 years, with significant difference between the groups.
2. The Bishop score was little bit favourable in the dinoprostone group before induction of labour.
3. The improvement in Bishop score was more with group A (misoprostol sublingually) than group B (those with dinoprostone gel) and was statistically significant with p values 0.00 and 0.001 at zero and at 4 hours.
4. Induction to delivery interval was shorter in sublingual Misoprostol group when compared to the dinoprostone gel applied intracervical.
5. Most of the participants delivered by normal vaginal delivery in both the groups.
6. When compared maximum number of LSCS was observed in misoprostol group.
7. The complication observed i.e. Meconium stained amniotic fluid was more in Misoprostol group.

8. Fetal distress was more in misoprostol group.
9. APGAR <7 and babies requiring NICU admission was more in Misoprostol group.
10. GI effects was observed more in dinoprostone gel group when compared to misoprostol group.
11. Postpartum Haemorrhage was more in the misoprostol group

CONCLUSION

CONCLUSION

From this study it has been observed that though there is no major difference between the group induced with misoprostol by sublingual route or in the group induced with Intracervical application of dinoprostone gel, the induction time is less in the group administered with sublingual misoprostol than dinoprostone and misoprostol given sublingually is having higher maternal febrile morbidity, higher rates of meconium stained amniotic fluid, fetal distress and NICU admission than intracervical dinoprostone gel induction and hence dinoprostone has much more promising advantage over the other in terms of fetal outcome. Thus it was concluded that though sublingual misoprostol is efficacious than intracervical dinoprostone, its safety margin is very less and hence misoprostol induction should be done only in a double setup under medical supervision.

ANNEXURE

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BIBLIOGRAPHY

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PROFORMA

NAME

AGE

IP NUMBER

OBSTETRIC SCORE

GESTATIONAL AGE

TIME OF RUPTURE OF MEMBRANES

HISTORY OF FEVER OR LABOR PAIN

PAST OBSTETRIC HISTORY

PAST MEDICAL OR SURGICAL HISTORY

GENERAL EXAMINATION

HEIGHT WEIGHT

PALLOR PEDAL EDEMA

PULSE RATE

BLOOD PRESSURE

PER ABDOMEN EXAMINATION

PER VAGINAL EXAMINATION

BISHOPS SCORE

ULTRASOUND

PRESENTATION

AFI

NON STRESS TEST

INVESTIGATIONS

MATERNAL TOTAL LEUCOCYTE COUNT

C-REACTIVE PROTEIN

MATERNAL MONITORING

HALF AN HOURLY PULSE RATE

4 HOURLY TEMPERATURE

PER ABDOMEN EXAMINATION

FHR MONITORING

PV FINDINGS AFTER INDUCTION

NUMBER OF PV EXAMINATIONS

FAILED INDUCTION

MODE OF DELIVERY

INDUCTION TO DELIVERY INTERVAL

PROM TO DELIVERY INTERVAL

APGAR SCORE OF BABY

ADMISSION IN NICU YES / NO

CONSENT FORM
PATIENT INFORMATION SHEET

I , Dr.Dharini.M , MS Post graduate in Obstetrics and Gynaecology and am conducting 'Comparative study of cervical ripening with sublingual misoprostol and intracervical dinoprostone gel in term prelabor rupture of membranes'. This study is to compare the safety and efficacy of sublingual misoprostol with intracervical dinoprostone gel for cervical ripening in term PROM and during the study you may need to undergo questionnaires ,lab investigations, ultra sound imaging and you will be induced with either sublingual misoprostol or intracervical dinoprostone gel. You and your baby will be monitored throughout the induction till delivery and in the event of any complications, appropriate actions will be taken. By participating in the above said study you will be helping to identify the safest and efficacious drug for cervical ripening in mothers with term rupture of membranes, thereby promoting inductions and reducing complications associated with it

Dr.Dharini.M
MS Post graduate in Obstetrics and Gynaecology
Thanjavur Medical college and Hospital,
Thanjavur

PARTICIPANT CONSENT FORM

Participants Name
Address :

Title of the study:

COMPARATIVE STUDY OF CERVICAL RIPENING WITH SUBLINGUAL MISOPROSTOL AND INTRACERVICAL DINOPROSTONE GEL IN TERM PRELABOR RUPTURE OF MEMBRANES

The details of the study have been provided to me in writing and explained to me in my own language. I confirm that I have understood the above study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without the medical care that will normally be provided by the hospital being affected. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purposes. I have been given an information sheet giving details of the study. I fully consent to participate in the above study

Signature of the participant : Date :

Signature of the witness : Date :

Signature of the investigator : Date:

ஒப்புகை படிவம்
நோயாளிகளுக்கான தகவல் படிவம்

மரு. மு . தாரிணி ஆகிய நான் அரசு ராஜா மிராசுதார் மருத்துவமனையில் மகப்பேறியல் மற்றும் பெண்ணோயியல் துறையில் முதலாம் ஆண்டு பட்டமேற்படிப்பு பயின்று வருகின்றேன்.நான் கர்ப்பிணி பெண்களுள் பிரசவ வலியின் முன்னரே பனிக்குடம் உடைந்துள்ளோறில் கர்ப்பப்பை வாய் பழுப்பதற்கு பயன்படுத்தப்படும் நாக்கின் அடியே வைக்கும் மிசோபுராஸ்டால் மற்றும் கர்ப்பப்பை வாயின் உள்ளே வைக்கும் டைனோப்ராஸ்டோன் மருந்துகளுள் ஒப்பிட்டு ஆய்வு நடத்த உள்ளேன். (Comparative study of cervical ripening with sublingual misoprostol and intracervical dinoprostone gel in term PROM). இதன் மூலமாக கர்ப்பப்பை வாய் பழுப்பதற்கு எந்த மருந்து சிறந்தது மற்றும் பாதுகாப்பானது என அறிய உள்ளேன்.இந்த ஆய்வின் போது கேள்வித்தொடருக்கு பதில் அளித்தல், ஆய்வக மற்றும் மருத்துவப் பரிசோதனைகள், அல்ட்ராசவுண்ட் இமேஜிங் போன்ற பரிசோதனைகள் தங்களுக்கு மேற்கொள்ளப்படும் மற்றும் கர்ப்பப்பை பழுப்பதற்காக நாக்கின் அடியே வைக்கும் மிசோபுராஸ்டால் அல்லது கர்ப்பப்பை வாயின் உள்ளே வைக்கும் டைனோப்ராஸ்டோன் மருந்து உபயோகிக்கப்படும். மேலும் பிரசவிக்கும் வரை நீங்களும் உங்களது குழந்தையும் கண்காணிக்க படுவீர்கள். ஏதேனும் பிரச்சினை ஏற்பட்டால் அதற்கேற்ற தீர்வு உடனே மேற்கொள்ள படும். இதனால் தங்களுக்கும் ஆரோக்யம் உறுதி செய்யப்படும் மேலும் இதுவிடயம் மேலே கூறப்பட்ட ஆய்வில் தங்களை உட்படுத்திக்கொள்வதனால் யாதொரு பாதிப்பும் ஏற்படாது என்பதனை தெரிவித்துக்கொள்கின்றேன் மேலும் இதில் பங்கேற்பதன் மூலம பிரசவ வலி முன்னரே பனிக்குடம் உடைந்து உள்ளோறில் சிறந்த மற்றும் பாதுகாப்பான மருந்து கண்டுபிடிக்க உதவி செய்து அதன் மூலம் பிரசவ வலி முன்னரே பனி க்குடம் உடைந்து உள்ளோறில் பிரசவ வலி ஏற்படுத்த மருந்து வைப்பதை ஊக்குவிக்கவும் அதனால் வரும் பிரச்சினைகளை குறைக்கவும் உதவுகிறீர்கள்.

மரு.மு. தாரிணி
மகப்பேறியல் மற்றும் பெண்ணோயியல் துறையில்
முதலாம் ஆண்டு பட்டமேற்படிப்பு மாணவி
அரசு ராஜா மிராசுதார் மருத்துவமனை,
தஞ்சாவூர் மருத்துவக் கல்லூரி,தஞ்சாவூர்.

பங்கேற்பவரின் ஒப்புகை படிவம்

பங்கேற்பவரின் பெயர்:
முகவரி :

விளக்கவுரை ஆய்வின் தலைப்பு:
கர்ப்பிணி பெண்களுள் பிரசவ வலியின் முன்னரே பனிக்குடம் உடைந்துள்ளோறில் கர்ப்பப்பை வாய் பழுப்பதற்கு பயன்படுத்தப்படும் நாக்கின் அடியே வைக்கும் மிசோபுராஸ்டால் மற்றும் கர்ப்பப்பை வாயின் உள்ளே வைக்கும் டைனோப்ராஸ்டோன் மருந்துகளுள் ஒப்பிட்டு ஆய்வு(Comparative study of cervical ripening with sublingual misoprostol and intracervical dinoprostone gel in term PROM).

இந்த ஒப்பிட்டு ஆய்வு குறித்த அத்துனை விடயங்களும், விளக்கங்களும் எனக்கு எழுத்துப்பூர்வமாகவும், வாய்மொழியாகவும் எனது தாய் மொழியில் நன்கு விளக்கி கூறப்பட்டது. மேலே கூறப்பட்ட ஒப்பிட்டு ஆய்வு குறித்து நான் நன்கு புரிந்துகொண்டேன் என்று உறுதி அளிக்கின்றேன்.மேலும் நான் இந்த ஒப்பிட்டு ஆய்வில் தன்னார்வத்தின் பேரில் யாருடைய கட்டாயமும் இன்றி கலந்துகொள்கின்றேன்.பின்வரும் காலங்களில் நான் இந்த ஆய்வில் இருந்து எனக்கு முறையே கிடைத்து வரும் சிகிச்சைகள் எவையும் பாதிக்காவண்ணம் எப்பொழுது வேண்டுமானாலும் சொந்தவிருப்பத்தின் பேரில் எந்த காரணமும் இன்றி விளகிக்கொள்ளலாம் என்பதனையும் நான் அறிவேன். இந்த ஆய்வில் கிடைக்கும் தகவல்கள் மற்றும் முடிவுகளை அறிவியல் சார்ந்த ஆய்விற்கு பயன்படுத்திக்கொள்ள நான் எந்த வகையிலும் தடைசொய்ய மாட்டேன் என்றும் இந்த ஆய்வு குறித்த நோயாளிகளுக்கான தகவல் படிவம் எனக்கு கொடுக்கப்பட்டது என்றும் இந்த ஆய்வில் என்னை ஈடுபடுத்திக்கொள்ள என்னுடைய பரிபூரண இசைவையும் ஒப்புதலையும் அளிக்கின்றேன்.

பங்கேற்பாளர் கையொப்பம்:
தேதி:
சாட்சியாளர் கையொப்பம்:
தேதி:
ஆய்வாளர் கையொப்பம் :
தேதி:

KEY TO MASTER CHART

Height:

1. <150cm
2. 151-160cm
3. 161-170cm
4. >170cm

Weight

1. <60kg
2. 60-65kg
3. 66-70kg
4. 71-75kg
5. >75kg

Gestational age:

1. 37-38weeks
2. 38-39 weeks
3. 39-40weeks
4. >40weeks

Parity

1 nulliparous

2 multiparous

Time since rupture of membranes

1 <2hours
2 2-4hours
3 4-6hours

PROM to delivery interval

1. <6hours
2. 6-12hours
3. >12hours

Bishops score

1. <2
2. 2-3
3. 3-4
4. 4-5

Duration of first stage of labour

1. <6hours
2. 6-10hours
3. 10-20hours
4. >20hours

Duration of second stage of labour

1. <1hour
2. >1hour

Mode of delivery

1 vaginal delivery
2 LSCS

LSCS indication

1 Failed induction
2 Failure to progress
3 Fetal distress
4 Others
5 Not applicable

C-reactive protein

1 positive

2 negative

Fetal heart rate monitoring

1 normal

2 indeterminate

3abnormal

NICU admission

1 yes 2 No

Complications

1 Meconium stained amniotic fluid
2 APGAR <7
3 NICU admission
4 Postpartum hemorrhage
5 pyrexia
6 Tachycardia for baby
7 GIT effects

MASTERCHART

S.No	age	ht	wt	ga	parity	rom	promtodel	bishop	stageone	stagetwo	modeofdelindlscs		crp	fhr	nicu	complictn
1	20	1	1	1	1	3	1	1	4	2	2	1	1	1	2	7
2	25	2	2	3	2	1	2	4	1	1	1	5	2	1	2	4
3	22	1	5	1	1	1	2	3	2	1	1	5	2	1	2	5
4	35	4	2	4	1	2	1	1	1	2	2	3	1	3	1	3
5	28	2	1	3	1	2	3	2	3	1	1	5	2	1	2	5
6	29	1	2	3	2	1	2	1	1	1	1	5	1	1	2	5
7	30	2	3	1	1	3	2	1	2	2	1	5	2	1	2	6
8	18	3	3	1	2	1	2	2	3	1	1	5	2	1	2	2
9	27	1	5	2	1	2	3	1	4	2	1	5	1	1	2	1
10	26	4	2	3	2	3	2	1	2	2	1	5	1	1	2	7
11	20	2	3	1	1	1	1	2	3	2	1	5	2	2	1	3
12	18	2	3	1	2	2	2	2	1	1	2	3	2	2	1	3
13	26	1	2	3	1	1	3	1	2	1	1	5	1	1	2	2
14	28	2	4	4	2	2	2	1	3	2	1	5	2	2	1	3
15	24	1	3	1	1	3	1	1	1	2	2	2	2	1	2	5
16	19	4	2	3	1	1	2	3	2	1	1	5	1	1	2	7
17	27	2	2	1	2	1	2	2	2	1	1	5	2	2	1	3
18	22	2	2	2	1	1	3	1	1	2	1	5	1	1	2	1
19	27	1	2	3	1	2	2	2	4	1	2	1	2	1	2	0
20	27	2	3	1	2	2	1	1	3	2	1	5	1	1	2	0
21	23	4	2	2	1	1	1	1	2	1	2	3	2	2	1	3
22	28	1	3	2	2	2	2	3	1	1	1	5	2	1	2	2
23	26	2	3	4	1	3	2	1	4	2	2	3	2	2	1	3
24	19	1	5	1	2	2	1	2	1	2	1	5	1	1	2	5
25	30	2	1	3	2	1	3	1	4	1	1	5	2	1	2	0
26	29	1	3	1	1	2	2	4	1	2	1	5	2	1	2	0
27	22	2	2	1	1	1	2	1	2	2	1	5	2	1	2	0
28	32	2	2	4	2	3	2	3	3	1	2	3	1	3	1	3
29	21	2	3	1	1	2	3	1	3	1	1	5	2	1	2	0

S.No	age	ht	wt	ga	parity	rom	promtodel	bishop	stageone	stagetwo	modeofdelindlscs		crp	fhr	nicu	complictn
30	22	2	2	4	1	2	2	2	3	2	1	5	2	1	2	1
31	18	1	5	2	1	1	3	1	4	1	1	5	2	1	2	6
32	28	4	3	3	1	1	2	1	1	1	1	5	1	1	2	4
33	23	2	1	3	1	1	2	2	2	2	1	5	2	1	2	2
34	19	1	4	3	1	2	3	1	4	2	2	2	2	1	2	0
35	28	2	2	3	1	2	2	1	1	1	1	5	1	1	2	0
36	27	1	4	4	2	1	2	1	4	1	1	5	2	1	2	0
37	31	2	2	1	1	2	2	3	3	2	1	5	2	1	2	5
38	19	4	2	2	1	3	3	2	1	1	1	5	2	1	2	5
39	26	2	2	4	2	2	2	2	2	2	2	2	2	1	2	0
40	21	2	4	1	1	1	3	2	1	1	1	5	2	1	2	5
41	29	2	3	4	2	2	1	1	4	2	1	5	1	1	2	0
42	19	3	3	3	1	1	3	2	3	1	1	5	2	1	2	0
43	29	2	4	1	1	3	3	1	2	2	1	5	1	1	2	3
44	27	2	2	2	1	2	2	2	1	1	1	5	2	1	2	0
45	18	3	3	1	1	2	3	3	3	1	1	5	1	1	2	7
46	34	1	2	4	1	1	2	2	2	2	2	2	1	1	2	7
47	22	4	2	3	1	2	2	2	2	1	1	5	2	1	2	0
48	19	2	3	2	2	1	2	1	1	1	1	5	1	1	2	5
49	31	2	3	1	1	2	2	2	3	2	2	3	2	3	1	3
50	18	2	1	3	1	2	3	1	1	1	1	5	2	1	2	5
51	25	2	5	2	2	1	2	1	2	2	1	5	1	1	2	0
52	26	2	3	2	1	3	2	3	4	1	2	1	2	1	2	0
53	21	2	2	1	1	2	1	2	2	2	1	5	2	1	2	0
54	31	2	3	3	2	2	2	1	1	2	2	3	1	2	1	3
55	28	2	3	2	1	1	2	4	2	1	2	3	2	2	1	3
56	24	2	3	3	2	2	2	1	2	1	1	5	2	1	2	5
57	19	2	3	2	2	1	1	1	3	2	1	5	1	1	2	1
58	21	2	4	4	1	2	2	2	1	1	2	4	1	1	2	5

S.No	age	ht	wt	ga	parity	rom	promtodel	bishop	stageone	stagetwo	modeofdelindlscs		crp	fhr	nicu	complictn
59	28	1	3	1	1	2	3	2	2	1	1	5	2	1	2	0
60	29	4	3	2	2	3	2	1	2	2	1	5	2	1	2	0
61	28	2	2	1	1	1	3	2	4	1	2	3	1	2	1	3
62	19	2	2	3	1	2	3	1	3	1	1	5	2	1	2	0
63	28	2	2	2	2	1	2	2	2	2	2	3	2	2	1	3
64	27	2	1	2	1	2	3	2	2	1	1	5	1	1	2	0
65	26	2	2	1	2	1	2	1	4	1	1	5	1	1	2	0
66	18	2	2	4	1	3	1	2	3	2	1	5	2	1	2	0
67	22	2	3	2	2	1	2	1	2	1	1	5	2	1	2	5
68	29	2	5	3	1	2	2	2	1	2	2	3	1	2	1	3
69	33	4	2	2	1	3	2	2	3	1	1	5	1	1	2	5
70	28	3	2	3	2	2	3	1	4	2	1	5	2	1	2	0
71	25	3	4	3	1	1	1	1	2	1	1	5	1	1	2	2
72	28	2	3	4	1	2	2	2	2	1	1	5	1	1	2	0
73	21	3	5	2	1	3	3	2	3	2	1	5	2	1	2	0
74	27	3	3	1	1	3	2	1	3	1	1	5	2	1	2	0
75	29	3	3	4	1	2	1	1	4	1	2	3	1	3	1	3
76	28	3	3	2	2	2	2	2	3	2	1	5	2	1	2	0
77	26	3	2	3	2	2	2	2	3	1	2	3	2	2	1	3
78	31	2	4	1	2	3	2	1	2	1	1	5	1	1	2	0
79	23	3	1	2	2	2	2	2	1	2	1	5	2	1	2	0
80	27	3	2	1	2	3	3	1	2	2	1	5	2	1	2	1
81	19	2	5	1	2	2	1	2	3	1	1	5	1	1	2	5
82	22	3	2	3	2	3	2	1	2	2	1	5	2	1	2	0
83	25	3	2	1	2	2	3	1	2	2	2	4	1	1	2	0
84	18	2	5	1	2	2	2	2	4	2	1	5	2	1	2	6
85	24	3	3	4	2	2	2	2	3	2	1	5	2	1	2	4
86	21	3	3	1	2	2	1	1	1	2	1	5	1	1	2	5
87	32	2	3	3	2	3	2	1	2	2	1	5	2	1	2	7

S.No	age	ht	wt	ga	parity	rom	promtodel	bishop	stageone	stagetwo	modeofdelindlscs		crp	fhr	nicu	complictn
88	23	3	4	2	2	3	1	2	3	2	2	3	2	3	1	3
89	25	3	5	1	2	3	2	1	4	2	1	5	1	1	2	1
90	22	3	3	3	2	2	2	4	2	2	2	3	2	3	1	3
91	26	3	2	1	2	2	3	1	3	2	1	5	2	1	2	2
92	21	3	3	4	2	2	2	2	3	2	1	5	2	1	2	5
93	18	3	2	3	2	3	1	1	2	2	1	5	1	1	2	0
94	26	3	3	2	2	2	2	1	4	2	1	5	2	1	2	1
95	34	3	3	1	2	3	2	2	2	2	2	3	2	2	1	3
96	27	3	2	2	2	2	1	2	4	2	1	5	2	1	2	5
97	22	4	4	4	2	2	3	1	3	2	1	5	1	1	2	7
98	28	3	1	3	2	3	3	2	1	2	2	3	2	3	1	3
99	28	3	3	1	2	2	3	1	3	2	1	5	1	1	2	0
100	19	3	2	3	2	3	2	4	3	2	1	5	2	1	2	0