"ORAL VERSUS VAGINAL ADMINISTRATION OF MISOPROSTOL, FOR INDUCTION OF LABOR, IN WOMEN PRESENTING WITH PREMATURE RUPTURE OF MEMBRANES." 1 YEAR RANDOMIZED CONTROLLED TRIAL AT KAHER'S DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELAGAVI

By

REG. NO. BJ0117007

Dissertation

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Endorsement by the HOD/Principal/ Head of the Institution

This is to certify that the dissertation entitled "**Oral versus vaginal administration of misoprostol, for induction of labor, in women presenting with Premature Rupture of Membranes."** 1 year Randomized Controlled Trial at KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi is a bonafide research work done by **Reg. no** B J 0 1 1 7 0 0 7 .

Dr. Kamal Patil **MD**
Professor and Head,
Department of Obstetrics,
And Gynecology ,
KAHER's
Nehru Nagar, Belagavi – 10
Date:
Place: Belagavi

Dr. N.S. Mahantashetti **MD**
Principal,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date:
Place: Belagavi

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(A constituent unit of KLE Academy of Higher Education & Research Deemed-to-be University)

Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category "A" by MHRD (GoI)

Nehru Nagar, Belagavi-590 010, Karnataka-India

Website : http/www.jnmc.edu
E-Mail : Principal@jnmc.edu

☎ Office :+91-(0)831 2471350
FAX :+91 (0)831-2470759

Ref. No. : MDC/PG/2628 Date : 22-10-2019

To,

REG. NO. BJ0117007
Postgraduate Student,
Department of Obst. & Gynecology,
2017-18 Batch,
J. N. Medical College,
Belagavi.

Sub: Acceptance Letter

Sir/Madam,

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Department of Obst. & Gynecology		Antiplagiarism Committee
J. N. M. C. Belagavi.		

ABBREVIATIONS

ACOG	- American College of Obstetricians and Gynaecologists
RCOG	- Royal College of Obstetricians and Gynaecologists
LSCS	- Lower segment caesarean section
SD	- Standard deviation.
CTG	- Cardiotochography
CS	- Cesarean Section
PROM	- Pre labour rupture of membrane.
LMP	- Last menstrual cycle
EDD	- Expected date of delivery
IOL	- Induction of labour
RCT	- Randomized controlled trial
FHR	- Fetal heart rate
ARM	- Artificial rupture of membranes
SRM	- Spontaneous rupture of membranes
OR	- Odds Ratio
C	I- Confidence Interval

ABSTRACT

"Oral versus vaginal administration of misoprostol, for induction of labor, in women presenting with pre labour rupture of membranes". 1 year randomized controlled trial at KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi.

AUTHORS: Dr. Vartika Mohan, Dr. Anita Dalal

INTRODUCTION: In patients presenting with Pre Labor Rupture of Membranes, Iduction of labour or augmentation of labor is preferred over expectant management, to reduce the duration of labor and to reduce the chances of complications like chorioamnionitis, neonatal infections, etc. Misoprostol has been recommended by the WHO for the purpose of IOL.[5]

OBJECTIVE: To compare the effectiveness of orally administered misoprostol, with vaginally administered misoprostol, for IOL in women with PROM. The mean interval between induction and active labor (cervical dilatation ≥4cm) and induction to delivery interval were compared between the two groups.

STUDY DESIGN: 1 year Randomized Controlled Trial

SOURCE OF DATA: All women presenting with PROM to the labor room of KAHER'S Dr. Prabhakar Kore Charitable Hospital, Belagavi.

STUDY PERIOD: 1 year (January 2018- December 2018)

METHOD: All women presenting with PROM, fitting the inclusion criteria, were enrolled after taking written informed consent and randomized. Each subject received 25 mcg of misoprostol 2nd hourly, orally or 25mcg misoprostol vaginally, 3rd hourly, for induction of labor. The time taken by each group to reach active labor (cervical dilatation ≥4cm) was compared.

RESULTS: The interval between the induction and active labour was found to be significantly shorter (4.7±2.1hours) as compared to the vaginal group (10.1±4.5hours). The interval between induction to delivery was also found to be significantly shorter in the oral group (8.9±3.5hours) as compared with that in the vaginal group (14.1±4.4hours), with similar rates of side effects in both the routes.

CONCLUSION: Oral misoprostol is a simpler, effective and more convenient route of administration as compared to the vaginal route for induction of labor in PROM.

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INTRODUCTION

The rupture of membranes at ≥ 37 completed weeks of gestation, before the spontaneous onset of labor, is defined as Pre labour rupture of membranes (PROM). [1,2] PROM at term complicates about 8%- 10% of pregnancies[1]. It has been noted that spontaneous labor begins within 12 hours of rupture of membranes in 50% of PROM cases, within 24 hours in 70% of PROM cases and within 48 hours in 48% of women with PROM. [1,2]

A prolonged time gap from the onset of rupture of membranes to that of delivery time is associated with a higher risk of infections in the mother (such as chorioamnionitis, post-partum endometritis and sepsis) and in the neonates.[3] In patients presenting with PROM, induction of labor or augmentation of labour should be preferred over expectant management to reduce the duration of labor and to reduce the chances of various associated complications like chorioamnionitis, neonatal infections, NICU admission, etc[2].

Results of the International Term PROM Trial suggest that prompt intervention in the form of induction of labor results in greater maternal satisfaction and a lower risk of maternal infection than expectant treatment".[2]

Induction of labor (IOL) is the process of stimulating uterine contractions artificially, before labor begins spontaneously. According to the WHO guidelines for IOL, women with PROM should be induced within 24 hours [4].

Oxytocin and prostaglandins are the two most frequently used pharmacological agents for induction of labor [5]. Oxytocin infusion is considered an effective method of labor induction with a good safety profile. However, the rate of successful induction is highly dependent on the ripeness of the cervix prior to induction [5]. Studies have shown that the use of an agent/ method for ripening of

cervix when used for induction of labor, shows a better response of oxytocin on the uterus once patient has gone into established labor[4,5].

Misoprostol is a synthetic analogue of prostaglandin E1 (PGE1). It is cost effective and is stable at room temperature. It has a long shelf life. Side effects include uterine hyperstimulation, hypertonus, tachysystole, fever, shivering, nausea and vomiting. It has been recommended by the WHO for the purpose of IOL.[5]

The efficacy and safety of misoprostol makes it a readily acceptable agent for induction of labor[4,5,6]. It can be used in place of I.V oxytocin infusion for IOL in women presenting with PROM, particularly in women with a poor pre induction cervical score[6]. Misoprostol is easy to administer and can be given via various routes- oral, buccal, sublingual, vaginal, rectal[6].

Many studies have been conducted comparing the effectiveness, safety profile, maternal and neonatal outcomes of oxytocin with that of misoprostol when used for induction in patients with PROM [7,8,9]. In these studies they found no significant difference in terms of the safety, efficacy and neonatal and maternal outcomes between the 2 groups.

However, the efficacy of oral misoprostol with that of vaginal misoprostol has not been sufficiently studied specifically in cases of PROM. The aim of this randomized controlled study is to compare the effectiveness of the oral route of misoprostol with that of the vaginal route of misoprostol when used for induction of labor in patients presenting with PROM with ≥37 completed weeks of gestation.

OBJECTIVE

Primary objective:

To compare the mean induction to active labor interval with oral and vaginal administration of misoprostol 25mcg.

Secondary objectives:

To compare:

a) The induction to delivery time.

b) The need for augmentation of labor with oxytocin.

REVIEW OF LITERATURE

Misoprostol is an effective and accepted method of inducing labour. There has been immense debate about the most appropriate dose as well as the best route of administration of misoprostol; oral vis-à-vis vaginal. The literature boasts numerous studies in the form of randomized trials as well as systematic reviews comparing the two.

A prolonged interval from rupture of membranes to delivery is associated with higher risk of maternal infection such as chorioamnionitis, postpartum endometritis, and sepsis[1]. A large randomized controlled trial on PROM compared IOL with oxytocin infusion and vaginal administration of prostaglandin E2 (PGE2) gel vs expectant treatment and showed that the two approaches were similar in terms of neonatal infections and cesarean section. However, the risk of maternal infection was lower in oxytocin induction compared with expectant treatment.[2]

ACOG guidelines, 2016 recommend active management after premature rupture of membranes[27]. But there was no evidence to recommend appropriate method of induction of labour in women with pre labour rupture of membranes[28].WHO in 2011 recommends traditional intravenous oxytocin for induction of labour for premature rupture of membranes[28].However induction with oxytocin needs continuous intravenous accesses and fetal monitoring and also restricts mobility even in early labour. Intra-vaginal prostaglandin E2 is other recommended method of choice which is less invasive and requires less amount of oxytocin than traditional oxytocin alone[28]. It is even approved by FDA for this purpose. But its cost and storage requirement makes its availability difficult especially for people in developing countries. Misoprostol an analogue of prostaglandin E1 has shown not only to be

effective in inducing labour but is also cheaper and stable at room temperature[29]. Misoprostol can be administered even orally which not possible with prostaglandin E2.

Misoprostol is a synthetic 15-deoxy-16-hydroxy-16-methyl analogue of prostaglandin E1. Various studies have shown both oral and vaginal misoprostol to be equally effective in cervical ripening and induction of labour[16,18,19,22,30.]

There are several studies comparing oral vs vaginal routes of misoprostol and few studies comparing oral versus sublingual, and vaginal vs sublingual routes for induction of labour. These studies have used different formulations and different doses. However, there is not substantial evidence to suggest the superiority of one route over the other in the clinical setting of PROM[12,14,16,18] .

Toppozada et al conducted a study wherein induction of labour was done in 40 women with term pregnancy by using misoprostol via two routes- oral and vaginal. The groups were equal in strength and were randomized. Group I received 100mcg misoprostol via vaginal route, every 3rd hourly while in group II, patients received the 100mcg misoprostol via oral route. Doubling of the dose was done in case of no response. This doubling was done under continuous FHR monitoring by cardiotocography (CTG). The authors found a shorter time interval in the vaginal group vis-à-vis the oral group, provided a low dose was used. Higher doses were seen to be associated with more abnormal FHR patterns and a higher rate of uterine hyperstimulation. It was recommended by the authors to use the vaginal route of misoprostol coupled with CTG monitoring of FHR.[7]

Few years later, in 2001, Shetty at al conducted a study wherein 245 pregnant women, who had indications for IOL, were term pregnancies and had unripe cervices were randomized to receive 50µgm misoprostol either via oral route or via vaginal

route, 4th hourly to a maximum 5 doses. The difference in mean interval between IOL and vaginal delivery was significant between the two groups, being shorter in the vaginal group (17.8hours versus 27.9hours). More women underwent delivery within 24 hours of induction and fewer number of women needed augmentation of labor with oxytocin (39% vs 58.2%) in the group which received misoprostol vaginally. No statistical differences were seen in the modes of delivery and the neonatal outcomes between the two groups. Similar to the findings of Toppozada et al, in this study too, the vaginal route of misoprostol was associated with higher incidence of uterine hyperstimulation as compared to the oral route. They concluded that for IOL, misoprostol has proven to be an effective pharmacological method. However, because the vaginal route was found to be associated with an increased incidence of uterine hyperstimulation and fetal distress, the oral route of misoprostol might can be chosen over the vaginal route.[8]

A similar study by Kwon et al conducted at around the same time looked at the induction to delivery time in 167 women in a randomized setting. Patients in the two groups received 50 μg of misoprostol orally or vaginally 6th hourly until the cervix became favorable for doing ARM or for SRM or they reached the stage of active labour. The mean interval between induction to delivery was lesser in the group which received vaginal Misoprostol (15.7 hours) as compared to the oral Misoprostol (23.0 hours) group. The mean number of doses required to make the patient reach the stage of active labor was also lower in the vaginal group. These results of the outcomes studied in this trial were statistically significant when the data was analyzed separately for primigravidas and multigravidas. No difference was seen in the two groups with respect to the uterine hyperstimulation and neonatal complications. There were more number of cesarean sections in the group which received vaginal

misoprostol as compared to the oral group. According to the authors, vaginal route of administering Misoprostol, for IOL at term, was found to have a shorter induction to delivery interval. Fewer doses of misoprostol were required per patient in the vaginal group. The rate of cesarean section was higher in the vaginal arm than the oral arm but this data was statistically insignificant.[9]

In a systematic review by Bartusevicius et al wherein PubMed, Cochrane Library and EMBASE searches were undertaken to look at controlled trials which compared different routes of administering Misoprostol for the purpose of IOL. This was published between 1994 and 2004. Seventeen studies were selected for this analysis. Compared to vaginal administration, oral route of Misoprostol was seen to have an association with higher rates of failed induction. The vaginal route was found to have fewer number of women who delivered via vaginal delivery within 24 hours of IOL (odds ratio- 1.61) and there was a higher rate of uterine hyperstimulation without accompanying FHR abnormalities (Odds Ratio 2.21, Confidence interval-95%) and the rate of cesarean section was lower (Odds Ratio- 0.74, Confidence interval-95%). Oral Misoprostol in lower dose (50 mcg) in comparison to 25–50 mcg dosage of misoprostol administered vaginally, had lesser women undergoing vaginal delivery within 24 hours of IOL, more need for augmentation with oxytocin, low incidence of uterine hyperstimulation and fewer women undergoing cesarean section. They concluded that vaginally administered misoprostol was seen to be a more effective labor inducing agent than an equal dose of orally administered misoprostol. However, when misoprostol was given vaginally, the risk of uterine hyperstimulation was seen to be higher.[10]

Fetiosa et al in 2006 reciprocated similar results in their RCT. It was a double-blinded randomized controlled trial. They compared sublingual versus vaginal

misoprostol. 150 women were recruited and randomization was done. Group 1- 25 mcg sublingual misoprostol every 6th hourly and the placebo was given vaginally. Group 2 received vaginal misoprostol (25mcg, 6th hourly) and placebo was given via the sublingual route. The data on outcomes of maternal interests and neonatal interests were analyzed. In the sublingual group, 57% women delivered vaginally and 69% women in the vaginal group delivered vaginally. The sublingual group had 11 cases of fetal distress while in the vaginal group, there were 4 cases of fetal distress. No significant differences were noted in the no. of doses of misoprostol needed in each group for IOL, time taken between the first dose of misoprostol to vaginal delivery, the rate of abnormal uterine contractility and neonatal outcomes. The authors concluded that sublingual misoprostol in the dosage of 25 mcg, 6th hourly was neither found to be superior nor inferior to the vaginal misoprostol, when compared in terms of effectiveness and safety.[11]

All the above studies included patients that had one or more indications for induction of labour. In 2002, at The Aberdeen Maternity Hospital, UK, a non-blinded, RCT was conducted by Shetty et al wherein they determined the benefit of misoprostol as an agent for induction vs conservative management in patients only with PROM. They compared induction of labor with orally administered misoprostol as a method of active management of PROM versus 24 hours of conservative management followed by IOL with oxytocin drip or IOL with PGE2 gel insertion. 61 women with PROM at ≥36 weeks of gestation were recruited and randomized into 2 groups. Group1 received 50 ug of oral misoprostol 4th hourly, up to a maximum of 5 doses (which was referred to as the active group). Group 2 received- PGE2 gel or oxytocin only, if the women didn't go into spontaneous labor till 24 hours after PROM (called as the conservative group). They concluded that the active

management of PROM in the oral misoprostol group had more women reaching the stage of active labor and undergoing vaginal delivery within 24 hours of PROM and had statistically no significant increase in maternal and neonatal complication. They also noted that the active management of PROM with IOL using oral misoprostol showed positive results of maternal satisfaction as compared with the expectant management.[12]

Roxane et al, conducted a retrospective study in an overweight population, evaluated whether cervical ripening with oral misoprostol increases cesarean delivery risk and prolongs time to vaginal delivery compared with vaginal misoprostol. The study was conducted in 2 phases. From 2013 to 2014, 138 women who needed IOL were induced with 25mcg vaginal misoprostol 4th hourly. In the second phase, from 2014 to 2015, 138 women were induced with oral misoprostol 50mcg 4th hourly. The data from both the phases was compared and analyzed. Their primary objective was to compare the rate of cesarean sections between both the groups. The rate of cesarean sections was found to be higher in the oral group. Women in the oral misoprostol group took a longer time to deliver vaginally in the oral group as compared with vaginal misoprostol group. Vaginal misoprostol group was seen to be more associated with the uterine tachysystole. They concluded that vaginally administered misoprostol is superior to orally given misoprostol in terms of lower rate of cesarean sections and a shorter time to vaginal delivery. Vaginal misoprostol was found to be a better pharmacological agent of IOL than oral misoprostol. However, the benefit of using vaginal misoprostol must be weighed against the complications associated with it such as uterine hyperstimulation which in turn leads to fetal distress and poor neonatal outcomes.[13]

Mehrotra et al in 2010, published a prospective study wherin they compared oral and vaginal Misoprostol in equivalent doses (50 µ gm) in terms of efficacy and safety for induction of labour. 128 term pregnancies were randomized into two groups to receive the same dose of Misoprostol i.e 50ugm, either orally or vaginally, 4th hourly until satisfactory contractions were achieved or a maximum of 200 µ gm dosage.

They found that the induction to delivery time was shorter in the vaginal group, however this did not achieve statistical significance. Not were the differences significant when comparing the modes of delivery, neonatal outcomes and maternal side-effects. However, the rate of abnormal uterine contractility of the uterus was seen to be more common in the group wich received misoprostol vaginally (10/68) as compared to that of the oral group, thus highlighting the need for careful FHR monitoring while using misoprostol through the vaginal route. [14]

A year later, Jindal Promila et al, in October 2011 conducted a double blinded RCT in Dayanand Medical College and Hospital, Ludhiana, India, with a primary objective of comparing efficacy and safety of 50 mcg vaginal misoprostol with that of orally given misoprostol, for the purpose of induction of labor. 110 women with term gestation were subjected to randomization, who had a pre-induction Bishop score < 4, for induction of labour, provided they had an indication for IOL. After randomizing, 51 women were given misoprostol orally and 52 women were given misoprostol vaginally, 4th hourly (maximum 6 doses) or till the woman achieved the stage of active labor (cervical dilatation >4), in both the groups.

They also found that the time between IOL and vaginal delivery was lesser in the vaginal group. Also, higher number of patients in the vaginal group had a successful induction.[15]

At around the same time, Rashmi, AnupPradhan et al, conducted a randomized controlled study which included all pregnant women presenting with PROM beyond 28 weeks of gestation at the Central referral Hospital, the teaching hospital of Sikkim Manipal Institute of Medical Science (SMIMS), Gangtok from December 2011 to December 2013. 140 women were subjected to randomizeation into 2 groups. Group1- received misoprostol 50 µg via oral route, 4th hourly (up to maximum 4 doses or maximum 200mcg dose). Group 2- received intravenous oxytocin infusion as per the hospital's protocol described as "intravenous infusion of oxytocin starting with a dose of 2mU/min with an incremental increase of 2mU/min every 30 min until adequate contraction, side-effects (hyperstimulation or fetal distress) or maximum infusion dose of 20 mU/min was achieved". The primary outcome was to analyze the time taken from induction of labour to vaginal delivery. They found that the mean interval between IOL to vaginal delivery was 5.0±2.58 hours in the oral misoprostol group as compared with 4.33±2.3 hours in the oxytocin group, which was just statistically significant and there were no statistical differences in the CS, gastrointestinal side effects and neonatal outcomes. [16]

A 2011, a meta-analysis review by Mozurkewich ELet al, at Division of Maternal-Fetal Medicine, University of Michigan, Ann Arbor, USA. 46 articles were reviewed in this study. Each of the included articles was assigned a "quality rating" and "strength of evidence rating." They found that the rate of patients delivering vaginally within 24 hours of induction of labor was higher in the women who had received Prostaglandin E2 (PGE2) and vaginally given misoprostol. They also noted that the incidence of uterine hyperstimulation was higher noted with them. Although, the incidence of uterine hyperstimulation was lower with mechanical methods of induction of labor as compared with PGE2 and misoprostol but the risk of maternal

and neonatal infections was increased as compared with the pharmacological methods. The authors concluded that the rate of women undergoing cesarean section and the incidence of uterine hyperstimulation were both lower in the oral misoprostol group as compared to the groups which received vaginal dinoprostone or placebo.[17]

In contrast, shortly before this, in 2008, Abbassi et al conducted a study in which 80 patients with term pregnancy, meeting the inclusion criteria, were recruited for IOL. Group 1 was given 50µ gm Misoprostol, by the oral route, 6th hourly and group 2 was given the same dose at the same interval via the vaginal route. The dose was repeated up to a maximum dose of 150 mcg. in the oral misoprostol group, the mean improvement in the Modified Bishop's Score was more after the first dose as compared to the vaginal route. The interval between IOL and delivery was shorter in the oral group than in the vaginal group. The need for augmentation with oxytocin was noted to be more in the vaginal group. The rate of vaginal deliveries was 95% in the oral group and 80% in the vaginal group. The dose-50 micrograms was found to be more effective in the oral group. No difference was seen between both the groups with respect to the analgesic requirement, instrumental delivery, maternal complications and neonatal outcomes. The authors concluded that safety and efficacy were not different in the low-dose vaginal and oral Misoprostol when used for the process of induction of labour. However, the oral misoprostol was found to be better with respect to the interval between induction and delivery, total number of doses of misoprostol required and the mode of delivery.[18]

In 2009, Sheikher et al, undertook a study to compare the effectiveness and safety of intra-vaginally administered Misoprostol, the oral route of Misoprostol and insertion of an intra- cervical catheter for the purpose of IOL at term. Each of the three groups was assigned 30 women with term pregnancy who were recruited for

IOL. The time taken from induction of labor to vaginal delivery, mode of delivery, Apgar score of the neonates & the rate of failed induction were analyzed. Women in the vaginal misoprostol group delivered vaginally fastest (10:35 hrs) as compared to those in the oral Misoprostol group and intra cervical catheter. The oral group and the Foley's Catheter group were associated with a lower risk of LSCS rate as compared to the vaginal group. Also, there were least number of cases of failed induction in the vaginal misoprostol group. The authors concluded that vaginally administered Misoprostol for the purpose of induction of labour was found to be a safe & an efficacious pharmacological method for labor induction with least number of complications. The study corroborated the efficacy & safety profile of vaginally administered Misoprostol in the dose of 25 µgm for IOL at term as compared to Orally given Misoprostol in the dose of 50 µgm and Intra-cervically inserted Foley's catheter.[19]

In 2003, Joan M G et al, had conducted a single blinded randomized controlled trial with an objective of comparing the effectiveness, safety profile and satisfaction of the patients of the oral route of misoprostol versus that with I.V infusion of Pitocin, for IOL in women with Prelabour rupture of membranes at term gestation. 105 women were stratified by their parity status. Then they were randomized and assigned to two groups- group 1 being oral misoprostol 75 µg every 4^{th} hourly or to group 2- being the one induced with intravenous oxytocin. They found that the time taken from induction to delivery was shorter [737 (±426) minutes] with I.V oxytocin as compared to737 (±426) minutes taken by women in the misoprostol group. This result reached statistical significance. The misoprostol group had a lower rate of uterine hyperstimulation as compared with the oxytocin group (misoprostol-6.0%, oxytocin-27.1%, p value- 0.005). Women were more satisfied in the

misoprostol group (misoprostol-86.0%, oxytocin-63.4%, p value -0.02). Their conclusion was that in women with PROM, at term gestation, management with oral route of misoprostol took a longer time from induction to vaginal delivery but the rate of maternal satisfaction was more in this group.[20]

In 2008, Cheng et al conducted a study in which women with gestation 34- 42 weeks, with an unfavorable cervix (Modified Bishop's score ≤ 6) and with an indication for IOL, were randomly assigned to receive either orally titrated misoprostol or vaginal Misoprostol. The orally titrated Misoprostol group received misoprostol according to a regimen described by the authors as 20 ml Misoprostol solution (1 microgram/ml) every hourly for 4 doses followed by titration as per the individual response of the uterus. The vaginal group received 25 mcg 4th hourly until their cervix became favorable. The primary outcome of the study was delivering vaginally within 12 hours of induction. Intention-to-treat method was applied for analyzing the data of the study. 75 (74.3%) women in the oral misoprostol group delivered vaginally within 12 hours and 27 (25.5%) women in the vaginal group. 11.3% cases had uterine hyperstimulation in the vaginal group as compared to none in the oral group. The titrated oral group had fewer neonates with <7 Apgar score at 1 minute of delivery as compared to the vaginal group. The authors concluded that in unripe cervix, misoprostol when given in titrated doses via the oral route had a lower rate of uterine hyperstimulation and cesarean sections than the vaginal Misoprostol.[21]

A 2014 Cochrane review was compiled by Alfirevic Z et al. They searched the Cochrane Pregnancy and Childbirth Group's Trials Register (January 2014) and two authors independently reviewed and assessed the data of these trials. Overall, there were 76 trials were included which had 14,412 women. Oral misoprostol with placebo was compared in 9 trials (1109 women). It was found that the women who were

induced with oral misoprostol were more likely to deliver vaginally within 24 hours of IOL and needed less augmentation with oxytocin.In 12 trials comparing the same outcomes with orally given misoprostol versus vaginal administration of dinoprostone gel in 3859 women, women in the oral arm were less likely to deliver by caesarean section. They found evidence of them having a slower rate of induction but no other differences were significant. Nine trials compared oral route of misoprostol with I.V oxytocin and the same outcomes were analyzed. CS rates were significantly lower in women who had received misoprostol via the oral route but the rates of meconium-stained liquor and fetal distress were more. Thirty-seven trials which included 6417 women which compared the oral route versus the vaginal route of administration of misoprostol, found that there weren't significant difference in the serious neonatal and maternal morbidity/mortality. The rate of interval between induction and vaginal delivery, hyperstimulation of uterus with FHR changes and the rate of caesarean section has heterogeneous association and this was related to the various dosage regimens, although they were lower in the oral misoprostol group. However, less number of babies born to mothers in the oral group had a low Apgar score. The incidence of PPH was lower in the oral group. The oral misoprostol group had an increased incidence of meconium-stained liquor. Overall, they concluded that the efficacy of misoprostol via the oral and the vaginal routes, is similar but since better perinatal outcomes are reported with the oral route, therefore they recommended it over the vaginal route.[22]

Rouzi et al, in 2014 conducted another randomized controlled trial at King Abdulaziz University, Saudi Arabia. The objective of their study was the comparison between hourly titrated oral misoprostol with vaginal dinoprostone insert.160 women were randomized into 2 groups. Group 1 received hourly titrated oral misoprostol and

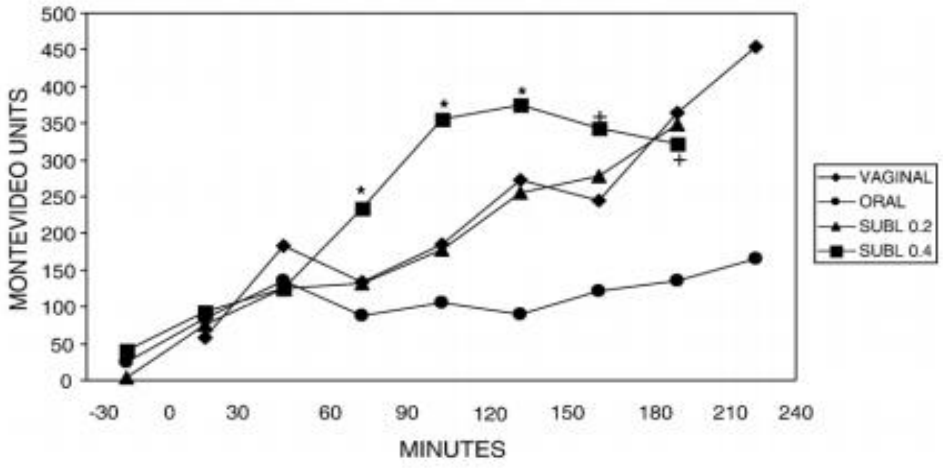
group 2 received Dinoprostone 10 mg vaginal insert. The primary outcome was the incidence of vaginal delivery within 24 hours of IOL. They found out that the number of women who underwent a vaginal delivery within 24 hours of induction was more for the nulliparas in the misoprostol group as compared with those in the dinoprostone group. More number of women who received misoprostol with a baseline Bishop's score of ≤3 were successfully induced as compared to the dinoprostone group. They concluded that hourly titrated oral misoprostol is an effective substitute to dinoprostone vaginal insert.[23]

Another recently published meta-analysis, in 2016, by Alfirevic L. et al, found that vaginally administered misoprostol in the dose of ≥50 μg is associated with a more vaginal deliveries occurring within 24 hours of IOL. Low dose of titrated oral misoprostol in the dose of < 50 μg is associated with a lower rate of caesarean deliveries.[24]

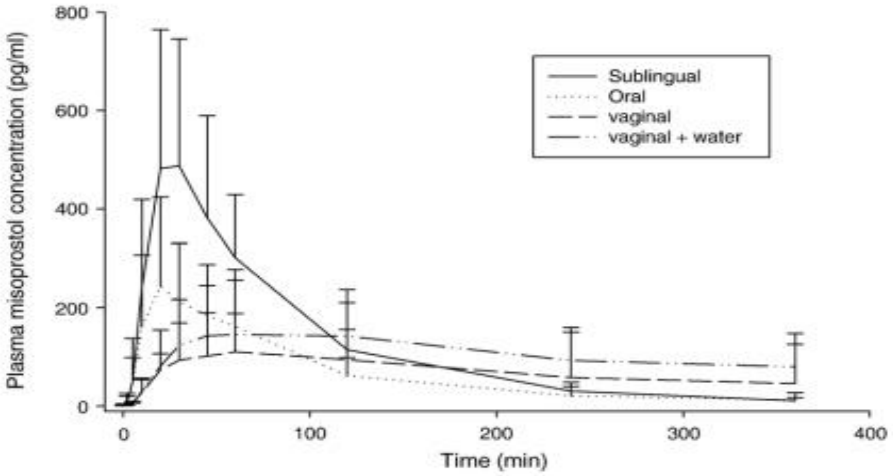
An open-label randomized controlled trial is being conducted in Araba University Hospital (Spain), by O. Lapuente-Ocamica et al, since 2016, with an objective of assessing which of the three therapeutic options (oral misoprostol, vaginal misoprostol and vaginal dinoprostone) has the highest rate of delivering vaginally within the 24 hours of induction of labour/drug administration. The statistical analysis of the study hasn't been publish yet since the study is still ongoing.[25]

Finally, a recently published meta-analysis in 2016, by Chen W et al, found out that the vaginal route of administration of misoprostol was the most efficacious pharmacological agent for ripening the cervix and resulting in vaginal delivery within 24 hours, but on the other hand,the incidence of uterine hyperstimulation with changes in the Fetal heart rate was found to be the highest in this group. The

incidence of uterine hyperstimulation along with FHR abnormalities in women who used a Foley's catheter for IOL was the lowest. The rate of caesarean section was found to be the lowest with orally administered misoprostol for the purpose of IOL. The authors concluded that misoprostol via the oral route, is a safe method for induction of labour than the vaginal route of misoprostol.[26]



This graph by Aronssonet al[31], depicts that the uterine contractions when measured in Montevideo units are stronger via vaginal route than those produced by the oral route. It is also noted in the graph, that the vaginal route produces strong contraction continuously as compared to the oral route.



Zeimanet al[36] found that the vaginal route of misoprostol has a slower rate of absorption with a gradual rise in the plasma concentration. It reaches the peak plasma concentration after 70-80 minutes and then declines slowly over 4 hours.

METHODOLOGY

The study was conducted in the labour room at KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi during the period from January 2018 to December 2018.

STUDY DESIGN – Randomized Controlled Trial.

STUDY PERIOD – 1 year (January 2018 – December 2018)

SOURCE OF DATA - All the confirmed cases of PROM, who got admitted to the labour room of KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi

SELECTION CRITERIA

INCLUSION CRITERIA –

Women with PROM in Latent Labor/ not in labor with

- Period of gestation ≥ 37 completed weeks
- Singleton pregnancy
- Reactive NST
- Vertex presentation
- Modified Bishop's score ≤ 6

EXCLUSION CRITERIA –

- Cervical dilatation ≥4 cm(in active labor) or modified Bishop's score ≥ 6
- Evidence of chorioamnionitis on admission(maternal tachycardia, fetal tachycardia, uterine tenderness, foul smelling discharge, fever)
- Placenta previa, abruption or unexplained vaginal bleeding
- Previous cesarean section or history of uterine surgeries like myomectomy, hysterotomy

- Associated obstetric co-morbidity, eg: severe pre eclampsia, Eclampsia, GDM with uncontrolled sugars
- Contraindications to the use of PGE1 analogues- previous known allergy / hypersensitivity to misoprostol.

ETHICAL CLEARANCE – The study was approved by the Ethical and Research Committee, KAHER'S Jawaharlal Nehru Medical College, Belagavi, prior to the commencement of this trial.

(Annexure 3 - Letter number MDC/DOME/71 dated 22/11/2017)

INFORMED CONSENT – All the participants fulfilling the selection criteria were explained about the purpose of the study and a written informed consent in their own vernacular language was obtained from all the participants before enrolment.

METHOD OF COLLECTION OF DATA

All the women who presented with a confirmed diagnosis of PROM, were enrolled in the study after taking written informed consent.

PROM was diagnosed on the basis of the following:

- On P/S examination- pooling of amniotic fluid in the vagina present
- On a detailed P/V examination- finding that membranes were absent
- A confirmed history of leaking per vagina since before admission

Inclusion criteria in addition to diagnosis of PROM, was checked for, in each subject and a pre induction score according to the Modified Bishop's score was documented.

The Modified Bishop's Score which was used:

Cervical feature	Pelvic score			
	0	1	2	3
Dilatation of cervix	<1cm	1-2cm	2-4cm	>4cm
Length of cervix	4cm	2-4cm	1-2cm	<1cm
Station of presenting part	-3	-2	-1/0	+1/+2
Consistency of cervix	Firm	Average	Soft	
Position of cervix	Posterior	Mid, ant.		

After enrolling the patients in the study, they were randomized into two groups and each of them was assigned a sequential study number in accordance with the sequential randomization technique. The sequence of numbers which was used for this randomization was prepared by a random number generator software.

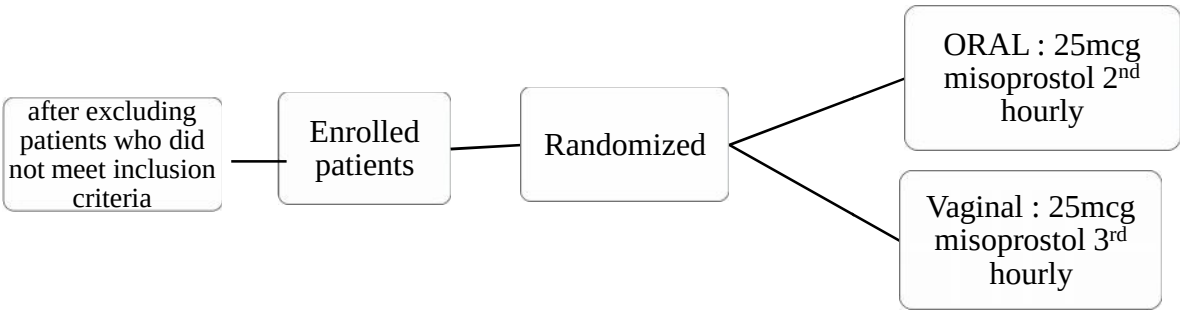
Each subject in group 1- received 25 microgram misoprostol 2nd hourly, orally up to a maximum of 12 doses or until adequate contractions ensued or till the patient reached active labor (cervical dilatation ≥4).

Group 2-receieved 25mcg misoprostol vaginally,3rd hourly, up to maximum 6 doses or until adequate contractions ensued or till the patient reached active labor (cervical dilatation ≥4), for the purpose of induction of labor. The time taken by each group to reach the stage of active labor (defined in the study as cervical dilatation ≥4) , the interval between induction and delivery and interval between onset of active labor and delivery, were recorded. The two groups were compared.

Failed induction was defined as the failure to establish

- labor, after one full regimen of 25mcg misoprostol 3rd hourly till max 6 doses and 25mcg misoprostol orally 2nd hourly till max 12 doses.

- Hypertonus was defined as a single uterine contraction lasting >120 seconds in an interval of 10 minutes.
- Tachysystole was defined as >5 uterine contraction, each lasting >40 seconds in 10 minutes.
- Hyperstimulation was defined as evidence of abnormal FHR along with either hypertonus or tachysystole.



STATISTICAL ANALYSIS:

Sample size formula:

The minimum sample size formula based on mean and standard deviation is

$$n = \frac{(z_\alpha + z_\beta)^2(s_1^2 + s_2^2)}{(\bar{X}_1 - \bar{X}_2)^2}$$

where z_α is the level of significance and z_β represents the power of the test. For 5% level of the significance z_α =1.96 and z_β =0.84 for 80% power of the test.

$\bar{X}_1$ is the mean of the first group (358) and $\bar{X}_2$ is the mean of the second group (573) {taken from parent article[15] }

s_1 is the standard deviation of the first group (308) and s_2 is the standard deviation of the second group (318).

With the above values the minimum sample size calculated is 40.

Note: This is the minimum sample size. To increase the power of the study, we have taken 50 cases in group 1 (oral group) and 46 cases in group 2 (vaginal group).

Statistical Analysis:

1. Categorical variables were represented in the form of numbers and percentage (%) and continuous variables were represented as mean ± SD
2. Comparison of the quantitative variables was done using Student T test between the two groups.
3. Chi- Square test and Fisher's exact test (2-tailed) were used for comparing the qualitative variables.

RESULT

This study was conducted at KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi between January 2018 and December 2018. A total of 317 women with PROM were admitted,of which 212 women were excluded since they did not meet the inclusion criteria. 105 women with PROM, meeting the inclusion criteria were screened. Out of these 105 women, 3 had fetal distress as seen on the admission CTG trace, 2 women were diagnosed to have anamnios on the admission USG scan and were taken up for an emergency LSCS and 1 woman did not give consent to participate in the study. A total of 96 women were recruited for the study and randomized into the two study groups- 50 in the oral group and 46 in the vaginal group.

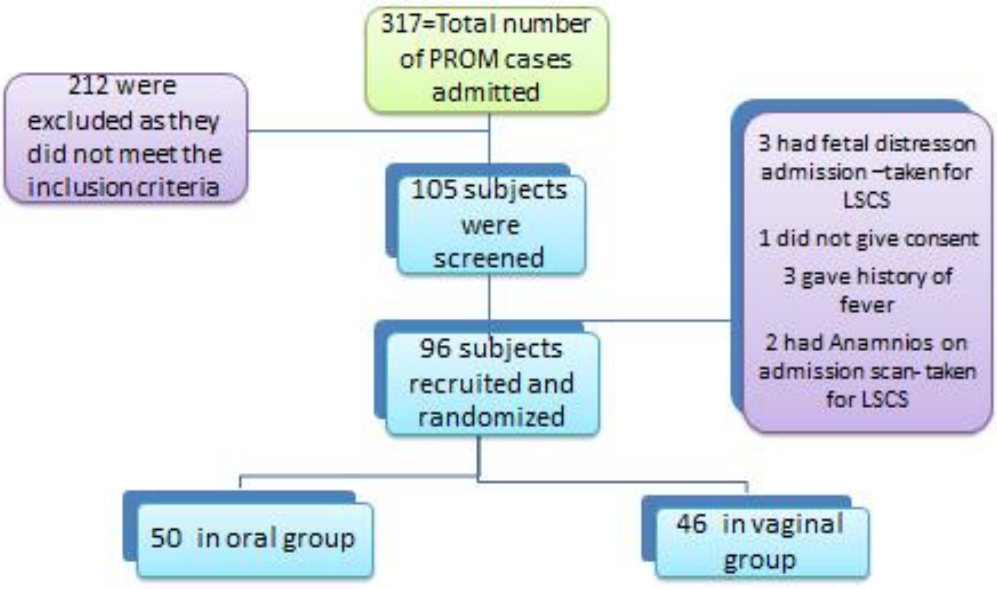


Table 1: Age Distribution in the study groups

Age (years)	Oral group N (%)	Vaginal group N (%)	P value
<20	5 (10%)	4 (9%)	1.980
20-30	43 (86%)	40 (87%)	1.302
>30	2 (4%)	2 (4%)	0.998

Graph 1: Age Distribution in the study groups

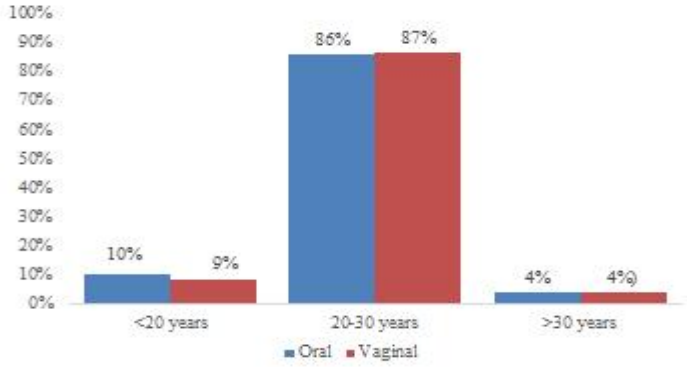


Table 1 shows the age distribution of women in the oral and vaginal groups. Majority of women were in the age group between 20 years- 30 years (oral group-43 (86%), vaginal group- 40 (87%).

Table 2: Registration status of women in the study groups

Registration status	Oral group n (%)	Vaginal group n (%)
Registered	32 (64%)	33 (72%)
Unregistered	18 (36%)	13 (28%)

p value 0.513

Graph 2: Registration status of women in the study groups

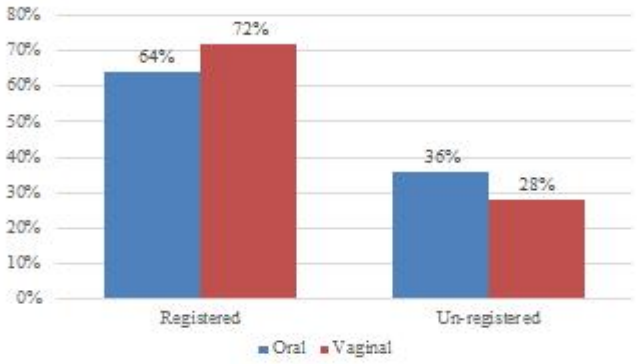


Table 2 shows the registration status of the women in both the groups. In the oral group -32 (64%) and in vaginal group -33 (72%) were registered cases.

Table 3: Distribution of women as per the Obstetric score

Obstetric score	Oral group n (%)	Vaginal group n (%)
Primigravida	16 (32%)	19 (41%)
Multigravida	34 (68%)	27 (59%)

P value – 0.399

Graph 3: Distribution of women as per the Obstetric score

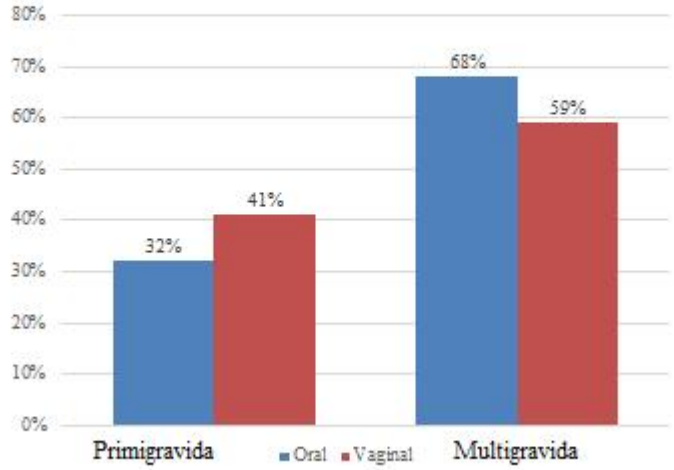


Table 3 shows the distribution of women as per their gravidity status in the study groups. Majority of women were multigravidas (34 (68%) in the oral group and 27 (59%) in vaginal group).

Table 4: Pre induction Modified Bishop's Score of the study groups

Modified Bishop's Score	Oral group n (%)	Vaginal group n (%)
0	1 (2%)	3 (6.5%)
1	1 (2%)	4 (8.7%)
2	13 (26%)	20 (43.5%)
3	20 (40%)	9 (19.5%)
4	13 (26%)	6 (13%)
5	2 (4%)	4 (8.7%)

P value 0.07

Graph 4: Pre induction Modified Bishop's Score of study groups

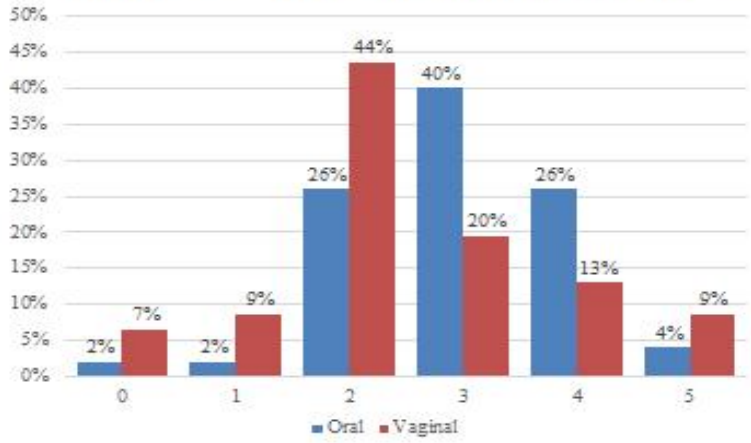


Table 4 depicts the pre induction modified Bishop's score of women in both the groups. Majority of the women in oral group (20 ; 40%) had a pre induction score of 3 while most of the women (20; 43.5%) in the vaginal group had pre induction score 2.

Table 5 : Mean duration of PV leak (in hours)at admission of the study groups

Variable	Oral	Vaginal	P value
Duration of PV leak (in hours)	7.1±2.8	6.7±2.9	0.835

Graph 5: Mean duration of PV leak (in hours) at admission of the study groups

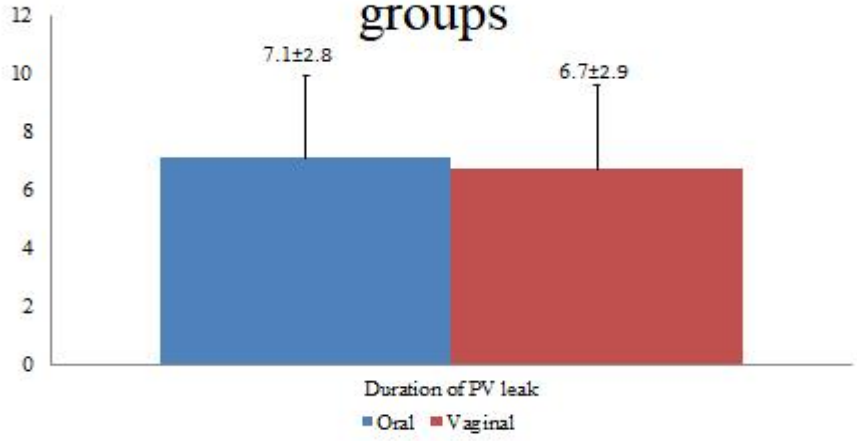


Table 5 depicts the duration of PV leak in hours, at admission. It was seen to be 7.1±2.8hours in the oral group and 6.6±2.9 hours in the vaginal group.

Table 6: number of doses of misoprostol needed in the study groups

Number of doses of 25mcg misoprostol needed	Route of administration		P value
	Oral n (%)	Vaginal n (%)	
1	6 (12)	5 (11)	1.000
2	18 (36)	9 (20)	0.111
3	14 (28)	8 (17)	0.235
4	5 (10)	6 (13)	0.753
5	4 (8)	13 (28)	0.076
6	2 (4)	5 (11)	0.231
10	1 (2)	0 (0)	1.000

.

Graph 6: Number of doses of misoprostol needed in study groups

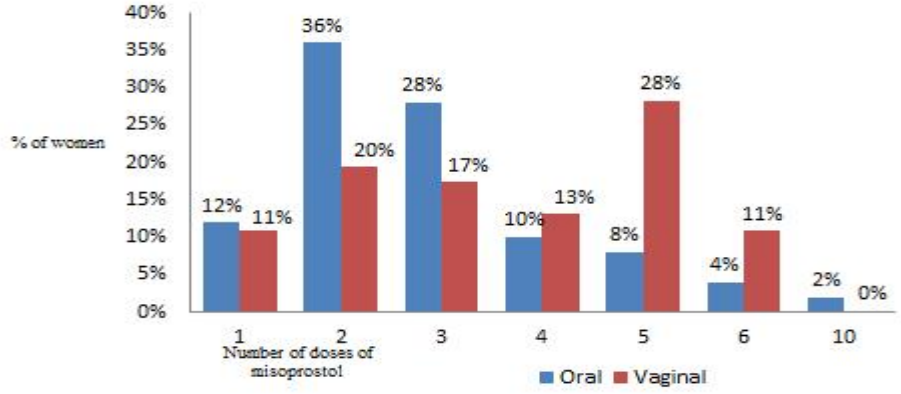


Table 6 represents the no. of doses of misoprostol required for successful induction in both the study groups. It was seen that most of the women 18(36%) in the oral group required 2 doses of misoprostol whereas most of the women in vaginal group 13 (28%) required 5 doses of misoprostol to enter into the stage of active labor.

Table 7: Proportion of women who required augmentation with oxytocin in the oral and vaginal group

Route of administration		Augmentation with oxytocin		P value
		n	%	
Oral	Primigravida	34	68%	0.399
	Multigravida	16	32%	
Vaginal	Primigravida	27	59%	
	Multigravida	19	41%	

Graph 7:Proportion of women who required augmentation with oxytocin in the oral and vaginal group

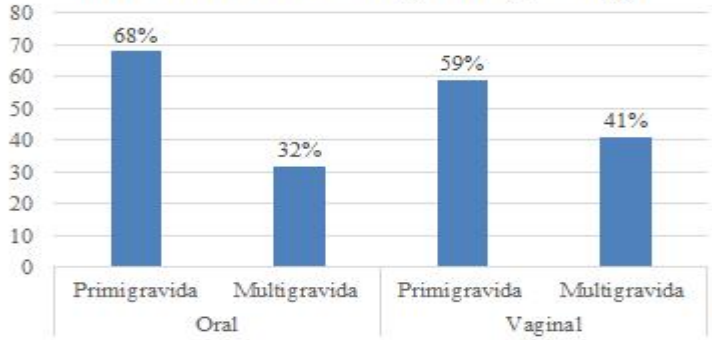


Table 7 depicts the proportion of women requiring augmentation with oxytocin in both the study groups. In the oral group 34 (68%) primigravidas and16 (32%) multigravidas required augmentation with oxytocin whereas in the vaginal group 27 (59%) primigravidas &19 (41%) multigravidas required augmentation with oxytocin.

Table 8: Incidence of Tachysystole in the study groups

Route of administration	Tachysystole (n=16)	
	n	%
Oral	7	14.0%
Vaginal	9	19.5%

P value - 0.586

Table 9 : Incidence of Hypertonus in the study groups

Route of administration	Hypertonus (n=2)	
	n	%
Oral	1	2.0%
Vaginal	1	2.2%

P value - 1.000

Table 10 : Incidence of Hyperstimulation in the study groups

Route of administration	Hyperstimulation (n=19)	
	n	%
Oral	9	18.0%
Vaginal	10	21.7%

P value - 0.798

- Table 8 depicts the incidence of tachysystole among women in the study groups and it was found that 9 (19.5%) women in the vaginal group experienced tachysystole while 7 (14%) in the oral group.
- Table 9 depicts the incidence of hypertonus among women in the study groups. It shows that there was 1 woman in ach group who experienced hypertonus (oral 2%, vaginal 2.2%)
- Table 10 depicts the incidence of hyperstimulation in women of the two study groups. In this, 10 (21.7%) women in the vaginal group and 9 (18%) women in the oral group experienced hyperstimulation.

Table 11 : Incidence of Failed Induction in both the groups

Route of administration	Failed Induction (n=3)	
	n	%
Oral	1	2.0%
Vaginal	2	4.3%

P value - 0.605

Table 11 shows the incidence of failed induction in both the study groups. There were 2 (4.3%) women in the vaginal group and 1 (2%) in the oral group who had failed induction.

Table 12 : Mode of delivery in the study groups

Route of administration	Mode of Delivery (n=96)					
	Instrumental Delivery		LSCS		Vaginal Delivery	
	n	%	n	%	n	%
Oral	4	8%	12	24%	34	68%
Vaginal	3	6.5%	15	32.6%	28	60.9%
P value	0.875		0.327		0.525	

Graph 8 : Mode of delivery in the study groups

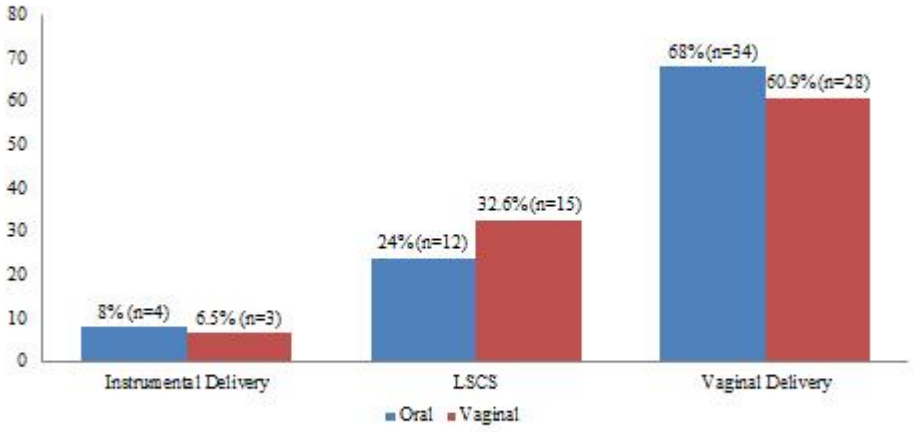


Table 12 depicts the various modes of delivery in the study groups. The rate of cesarean section was higher in the vaginal group [15 (32.6%)] than in the oral group [12 (24%)]. On the contrary, more no. of women in the oral group delivered vaginally [34 (68%)] as compared to in the vaginal group [28 (60.9%)]. There were 4 (8%) women in the vaginal group and 3 (6.5%) women in the oral group who had an instrumental delivery.

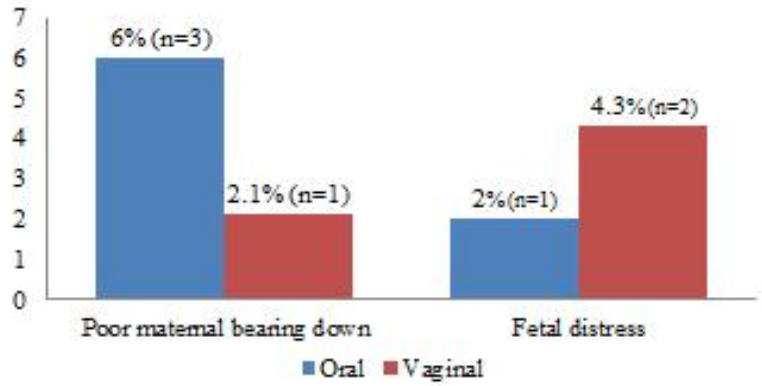
Table 13: Indications of instrumental delivery and LSCS in the study groups

	Indications	Oral	Vaginal	P value
Instrumental vaginal delivery	Poor maternal bearing down	3 (6%)	1 (2.1%)	0.618
	Fetal distress	1 (2%)	2 (4.3%)	0.605
LSCS	Failed induction	1 (2%)	2 (4.3%)	0.605
	Fetal distress	9 (18%)	12 (23.9%)	0.462
	Prolonged PROM (>24rs)	2 (4%)	1 (2.2%)	0.871

Table 13 represents the indications of instrumental delivery and Indications of LSCS in both the groups.

- Indications of instrumental vaginal delivery in the oral group were- poor maternal bearing down efforts 3 (6%) and fetal distress 1(2%) and indications of instrumental vaginal delivery in the vaginal group were- 1 (2.1%) poor maternal bearing down efforts and 2(4.3%) fetal distress.
- Indications of LSCS in the oral group were- failed induction 1(2%), fetal distress 9(18%), Prolonged PROM 2(4%). Indications of LSCS in vaginal group were- failed induction 2(4.3%), fetal distress 12(23.9%), Prolonged PROM 1(2.2%).

Graph 9: Indications of instrumental delivery in the study groups



Graph 10: Indications of LSCS in the study groups

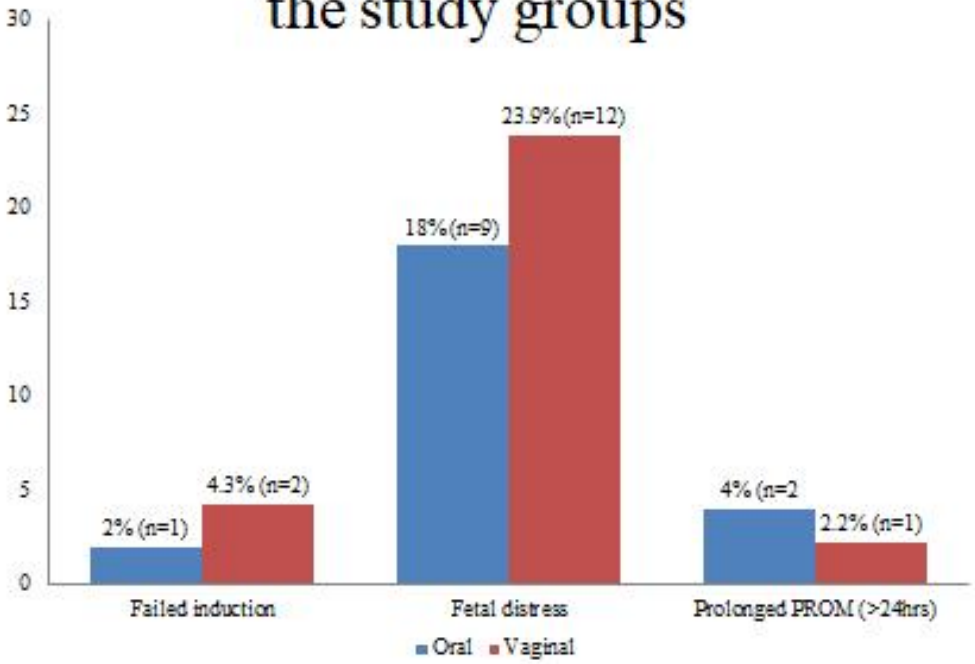


Table 14: Mean Induction to Active Labor interval (in Hours) in the study groups

Route of administration	Induction to Active Labor (Hours)
Oral group	4.7±2.1
Vaginal group	10.1±4.5

P value <0.0001

Graph 11: Mean Induction to Active labor interval (hours) in the study groups

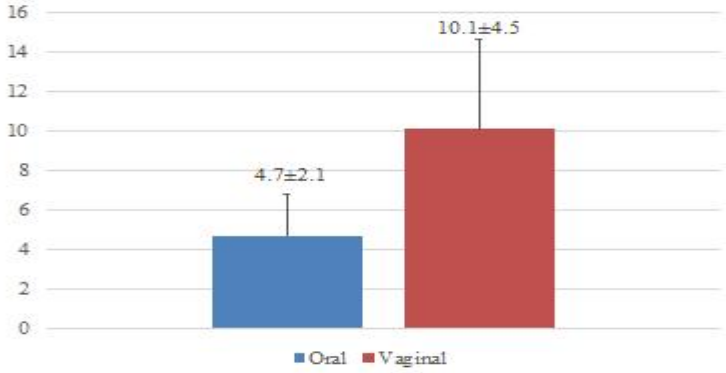


Table 14 represents the mean interval between induction and active labor in hours. It shows that the women in the oral group took a shorter time interval from induction to reach active labor (4.7±2.1 hours) as compared to the women in the vaginal group (10.1±4.5 hours).

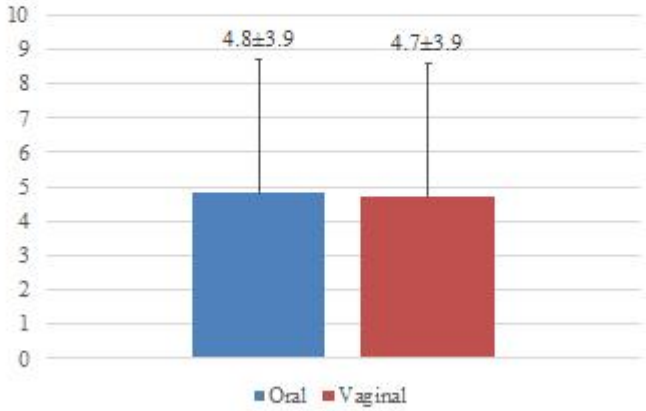
Table 15: Induction outcomes in the study groups

Route of administration	Induction to delivery interval (hours)	Active labor to delivery interval (hours)
Oral group	8.9±3.5 hours	4.8±3.9 hours
Vaginal group	14.1±4.4 hours	4.7±3.9 hours
P value	<0.0001	0.901

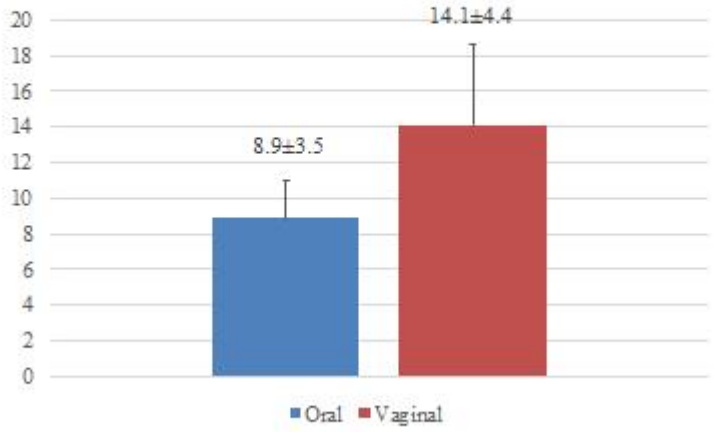
Table 15 depicts the two induction outcomes studied in this trial.

- The mean induction to delivery interval in hours was seen to be shorter in the oral group (8.9±3.5 hours) as compared to the vaginal group (14.1±4.4 hours).
- The mean time interval between active labor stage and delivery in hours, was 4.8±3.9 hours in the oral group and 4.7±3.9 hours in the vaginal group.

Graph 13- Mean Active labor to delivery interval (hours) in the study groups



Graph 12- Mean Induction to delivery interval (hours) in the study groups



NEONATAL OUTCOMES

Table 16- Birth weight of neonates in the study groups

	Birth weight (kg) (n=96)			
	< 2.5	2.5 - 3	3.1- 3.5	>3.5
Oral group	15 (30%)	28 (56%)	5 (10%)	2 (4%)
Vaginal group	10 (22%)	27 (58%)	6 (13%)	3 (6%)

P value – 0.766

Graph 14: Birth weight of neonates in the study groups

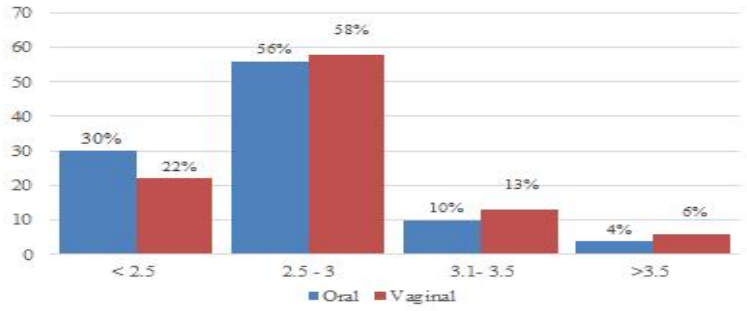


Table 16 depicts the birth weight of neonates in both the study groups. In both the groups majority of the babies [oral-28 (56%), vaginal 27 (58%)] were born with a birth weight between 2.5- 3kg.

Table 17: APGAR Score of neonates in the study groups

	Oral group	Vaginal group
APGAR at 1 minute	6.3±0.7	6.1±0.6
APGAR at 5 minutes	7.5±0.7	7.2±0.6

Graph 15: APGAR Score of neonates in the study groups

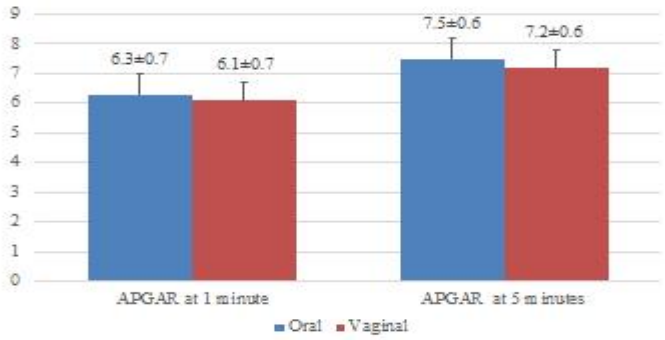


Table 17 depicts the APGAR score of the neonates born in both the study groups; 1minute after birth and 5 minutes after birth. In the oral group the mean APGAR score at 1 min of birth was 6.3±0.7 and it was 6.1±0.6 in the vaginal group. The mean APGAR score at 5 minutes of birth was 7.5±0.7 in oral group and 7.2±0.6 in the vaginal group.

Table 18: NICU Admissions with indications in the study groups

	Oral group n (%)	Vaginal group n (%)	P value
NICU Admissions	7 (14 %)	5 (10.8 %)	0.354
Indications :			
Respiratory distress	1 (2%)	2 (4.3%)	0.605
Low birth weight	3 (6%)	1 (2.2%)	0.618
Kangaroo mother care	3 (6%)	2 (4.3%)	0.872

Graph 16: NICU admissions with indications in the study groups

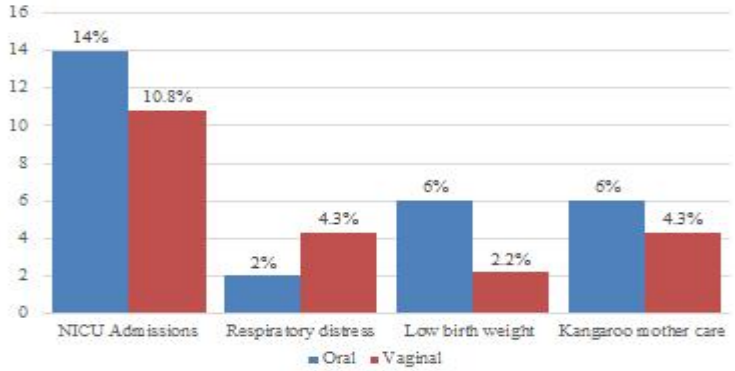


Table 18 represents the various indications of NICU admissions of neonates in the study groups.

- Indications of NICU admissions in the Oral group were- respiratory distress 1 (2%), low birth weight 3 (6%), KMC ward 3 (6%).
- Indications of NICU admissions in the Vaginal group were- respiratory distress 2 (4.3%), low birth weight 1 (2.2%), KMC ward 2 (4.3%).

DISCUSSION

This randomized controlled trial was conducted at KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi, between January 2018 and December 2018. A total of 317 women with PROM were admitted during the study period out of which 212 were excluded since they did not meet the inclusion criteria and 105 women were screened in the study. Out of which 96 women were recruited and randomized into the two study groups. This study compared various outcomes after administration of misoprostol like the time taken from induction to reach active labor, induction to delivery interval, number of patients requiring augmentation of labor with oxytocin, incidence of hyperstimulation, hypertoncicity, tachysystole, failed inductions, need for instrumental delivery and C sections, number of doses of misoprostol needed for induction of labour in patients with Pre-labour Rupture of Membranes at Term.

In this study the demographic variables were comparable between the two groups. In table 1, it was observed that most of the women who were recruited in this study were in the age group of 20 years to 30 years in both the study groups [oral- 43 (86%) and vaginal- 40 (87%)]. This result was similar to the other studies in which women of the study groups were also in the age group of 20-30 years.[10,11,15]

The ANC registration status of the women (depicted in table 2) recruited in this study was also comparable- [32 (64%)] of the subjects in the oral group and [33 (72%)] in the vaginal group were registered cases. This result was similar to the other studies [10,11,15].

Another comparable variable was the parity status (shown in table 3) of the recruited subjects in the study. It was found that most women were primigravida in

both the groups – [34 (68%)] in the oral group and [27 (59%) in the vaginal group. This result was similar to the other studies [10,11,15].

On evaluating the pre induction score according to the Modified Bishop's Criteria (shown in table 4), it was found that there was no statistical difference between the two groups (p value 0.06). 40% in the oral group had a pre induction modified bishop's score of 3 and 43.5% in the vaginal group had a pre induction modified bishop's score of 2. This was similar to other studies [13,17].

As depicted in table 5, the duration of PV leak (in hours), on admission, of the recruited patients was analyzed in this study. It was found to be comparable in the two groups: 7.1±2.8 hours in the oral group and 6.7±2.9 hours in the vaginal group, with a p value of 0.835. this represents that the two groups were comparable in terms of the duration of PROM.

In table 6, it was seen that fewer number of doses of misoprostol were needed in the oral group (2.9±1.6) as compared to those needed in the vaginal group (3.6±1.6) but this difference was not statistically significant with a p value of 0.068. Contrary to our findings, Jindal Promila et al, in 2011 found in their study that the vaginal group receiving 50 mcg misoprostol 4th hourly, needed lesser number of doses (2 (1–6)) as compared to the oral misoprostol group (6 (1-6))which received the same strength of misoprostol as the vaginal group[15]. Sharma DD et al, in 2019 found in their study, that 39% subjects in the vaginal group receiving 25 mcg misoprostol 4th hourly required more than 2 doses while 58% subjects in the oral misoprostol group receiving 50 mcg misoprostol 4th hourly needed more than two doses, for successful induction[30].

This difference in results between this study and the studies mentioned above, could be due to the less frequent doses of oral misoprostol. This study has used 25 mcg oral misoprostol given 2nd hourly and 25mcg vaginal misoprostol 3rd hourly.

However, in the study by Sharma DD et al, 50 mcg of misoprostol was given 4th hourly orally as well as vaginally, up to a maximum of 5 doses[30]. In the study conducted by Jindal Promila et al, 50 mcg of misoprostol was given every four hourly(maximum six doses)in both oral or vaginal groups[15]. We are of the opinion that, since, in our study, oral misoprostol was given more frequently as compared to the other studies, the plasma concentration of misoprostol could have been maintained throughout and hence the better result on the uterine activity can be explained. No studies are available which used the exact same dosage regimens for oral and vaginal routes of misoprostol for comparison.

In the present study, the augmentation with oxytocin (shown in table 7) was found to be more in the oral group [43 (86%)] as compared to the vaginal group [38 (82.6%)] but this difference was statistically not significant with a p value of 0.781. The findings of the present study were in conjunction with the study conducted by Shetty et al, in which the two groups had received 50mgm of misoprostol orally or vaginally four hourly to a maximum of 5 doses. The oral group needed more augmentation with oxytocin (71 {58.2}) as compared with the vaginal group (48 {39}) and this difference was statistically significant with a p value of 0.005[8]. A few years earlier, Roxane C et al had conducted a randomised controlled trial, comparing oral vs vaginal routes of misoprostol for induction of labour and risk of caesarean delivery as their primary outcome. They had administered 25 mcg misoprostol vaginally 4th hourly upto a maximum of 6 doses and 50 mcg orally 4th hourly upto a maximum of 6 doses. They too found that more subjects in the oral group needed augmentation with oxytocin [120 (87%)] while the vaginal group had a lower rate of augmentation with oxytocin in comparison [110 (79.7%)] and this difference was statistically significant[13].

This difference can again be explained on the basis of the frequency of administration of oral misoprostol, which was more scattered in the above mentioned studies.

Tables 8, 9, 10 depict the incidence of tachysystole, hypertonus and hyperstimulation in the two groups, respectively. It was found that 9(19.5%) subjects in the vaginal group had tachysystole as compared to the oral group, in which 7(14%) had tachysystole. This was statistically not significant. Similar results were seen while comparing the two groups for the occurrence of hypertonus (vaginal group- 1(2.2%) and oral group (1 (2%) and that of hyperstimulation (vaginal group- 10(21.7%) and oral group- 10(21.7%) and the two were statistically insignificant. A study by Cheng et al[21] showed that there were no cases of uterine hyperstimulation in the oral group as compared to 11.3% incidence of uterine hyperstimulation in the vaginal group. It was statistically significant.

A 2014 Cochrane review was compiled by Alfirevic Z et al. They studied thirty-seven trials comprising 6417 women, where the oral and vaginal routes of misoprostol administration were compared. They found that the incidence of uterine hyperstimulation along with fetal heart rate (FHR) abnormalities and the rate of caesarean deliveries, had a heterogeneous association and this was related to the dosage regimens. They were found to be lower in those with lower doses of oral misoprostol[22].

Aronsson et al[31], studied the strength of uterie contractions produced by various routes of misoprostol and they found that the uterine contractions when measured in Montevideo units were stronger in the vaginal route (maximum being 450 MU) than those produced by the oral route (maximum 150 MU)[31]. This finding may be able to explain the more number of subjects experiencing uterine hypertonus,

tachysystole and hyperstimulation in the vaginal group. It was also seen that the uterine contractions were continuously stronger in the vaginal group whereas they were weaker but more frequent in the oral group. This again explains the higher incidence of uterine side effects in the vaginal group.

As depicted in table 11,the present study showed that the oral group had 1 (2%) case of failed induction whereas the vaginal group had 2 (4.3%) cases of failed induction. The p- value being 0.605, therefore, rendering this difference statistically non-significant. The various studies comparing oral and vaginal routes of misoprostol have reported heterogeneous results with respect to failed induction.

These results were in conjunction with the results of the trial conducted by Sharma DD et al[30]. In their study the oral group had 9 cases of failed induction as compared to the vaginal group which had 12 cases of failed induction but this wasn't statistically significant (p vale 0.73). However, Roxane C[13] et al found that the oral group in their study had 25 (18.1%) failed inductions whereas the vaginal group had only 12(8.7%) failed induction cases, with a statistically significant difference.

In the present study, table 12 depicts the various modes of delivery of the women in the study groups. 12 (24%) subjects underwent emergency LSCS in the oral group while 15 (32.6%) in the vaginal group. More number of LSCS were seen in the vaginal group when compared with the oral group but this difference was statistically not significant (p value- 0.567). More number of women from the oral group [34 (76%)] delivered vaginally as compared to the vaginal group [31 (67.3%)]. This outcome of vaginal delivery was also not statistically significant (p value- 0.489). Out of these, 4 (8%) women had an instrumental delivery in the oral group while 3(6.5%) women in the vaginal group and this result was also statistically insignificant (p value-0.87). The incidence of LSCS was found to be more in the vaginal group 15

(32.6%) as compared to the oral group i.e. 12(24%), however this was statistically insignificant. The indications in the oral group and vaginal group were comparable and statistically not significant.

Table 13 depicts the various indications of LSCS and instrumental delivery in both the study groups. The indication of LSCS in the 12 subjects of the oral group were- failed induction (n=1, 2%), fetal distress (n=9, 18%) out of which, the cause of fetal distress was hypertonicity of the uterus in 1 case and prolonged PROM in 2 (4%) cases. In the vaginal group 15 cases underwent emergency LSCS and their indications were- failed induction (n=2, 4.3%), fetal distress (n=12 ,23.3%), out of which, the cause of fetal distress was hypertonicity of the uterus in 1(2.2%) and 1 (2.2%) was due to prolonged PROM. A few other similar studies have found contrasting results with regard to the delivery outcomes in the two groups.

These results were similar to the results of the trial conducted by Sharma DD et al[30]. They found that 76% subjects in the oral group delivered vaginally as compared to 72% in the vaginal group, which was statistically not significant (p value 0.41). There was no statistical difference in the rate of LSCS in both the groups [oral- 18% & vaginal- 20%; p value 0.88]. Similar results in the rate of instrumental delivery [oral- 06% & vaginal- 08%; p value 0.73]. On the contrary, Roxane et al[13] found that the rate of LSCS in their study was more in the oral group (31.9%) than in the vaginal group (21%) and this result reached statistical significance. Shetty et al[8] had found in their study too that the rate of LSCS is higher in the oral group [30(24.6%)] than in the vaginal group [28(22.8%)]. Such contrasting results may be explained on the basis of varying dosage and frequency schedules as used in the various studies.

The primary objective of the present study (represented in table 14) was to compare the interval between the time of induction and the onset of active labour, in the two groups. It was observed that the oral group reached active labour faster (4.7 ± 2.1 hours) than the vaginal group (10.1 ± 4.5 hours) and this difference between the two groups reached statistical significance (p value < 0.0001). On the contrary, Jindal Promila et al, found in their study that the oral group took longer to reach active labour (9.25 hrs) as compared with the vaginal group (which took 6hrs, p value 0.0045) and this finding reached statistical significance[15]. Not many studies have analysed this particular outcome.

Table 15 depicts the secondary outcome which was to compare the induction to delivery interval. The present study found that the oral group had a shorter interval between induction and delivery (8.9±3.5 hours) as compared to the vaginal group (14.1±4.4 hours). This result was of statistical significance (p value <0.0001). Negating our findings, Sharma DD et al found in their study that the oral group took longer than the vaginal group from induction to delivery and their result did reach statistical significance (oral- 23.3±12.4 hours , vaginal- 17.3±10.9hours, p value 0.0014)[30]

Jaince et al, in their study had seen that the oral group had longer induction to delivery times (oral- 27.3 hours, vaginal-19.3hours) than the vaginal group but their result was not statistically significant[32]. Similarly, Jindal Promila et al found that the oral group was taking longer than the vaginal group and their result was statistically significant (oral- 16.47hours, vaginal- 9.79 hours)[15]. Another study by Rehman et al found similar results that the oral group had longer induction to delivery times (oral- 21.22±2.4 hours, vaginal group- 20.15±3.1 hours) but this result did not reach statistical significance[33]. All the mentioned studies used 50 mcg misoprostol orally

4thhourly, whereas 25mcg or 50mcg misoprostol vaginally 4th hourly. While our study used oral misoprostol 25 mcg, 2nd hourly and 25mcg misoprostol vaginally 3rd hourly in PROM cases. We believe that we were able to maintain a constant level of misoprostol in both the groups throughout the induction process and owing to a higher peak plasma concentration of orally given misoprostol, this group experienced constant uterine activity and hence took a shorter interval between induction and delivery. This observation is supported by a studies conducted by O S Tang et al[34] and Zeiman et al[36]. The difference in the results of the above mentioned trials and our study can be explained on the basis of the dosing schedule of oral misoprostol and vaginal misoprostol used in the studies.

O S Tang et al[34], studied the pharmacokinetics of misoprostol through its various routes of administration. They found that through the oral route, misoprostol gets absorbed rapidly and almost completely from the GIT. It then undergoes de esterification (extensive first pass metabolism) and forms an active ingredient called misoprostol acid. This results in a sudden increase in the uterine tone within 30 minutes Aronsson A et al[31], Norman et al[35] (which corresponds to the peak plasma concentration which is reached in 30 minutes) but regular uterine contractions don't ensue because misoprostol acid gets cleared out completely within 120 minutes unless repeated doses are given.

Zeiman et al[36] found that the vaginal route of misoprostol results in a slower absorption of the drug with a gradual rise in the plasma concentration. It reaches the peak plasma concentration after 70-80 minutes and then declines slowly over 4 hours. It is able to produce regular uterine contractions after the initial increase the uterine tone since it maintains a constant plasma level till 6 hours after administration. This is

because it bypasses the first pass metabolism but this plasma concentration is lower than that of the oral route[36].

They also commented that the vaginal tablet of misoprostol has an inconsistent absorption. This was attributed to the practical observation of finding remnants vaginal tablets of misoprostol in the vagina, hours after administration, the faulty technique of inserting the tablets, or in our case finding that the soluble vaginal tablets get washed off from the vagina along with the leaking liquor amnii. This indicates that the absorption via the vaginal route is variable and incomplete. It can also be because of the varying vaginal pH and vaginal discharge, excessive show, etc of different women receiving the vaginal tablets[34].

On the other hand, it has been found that the absorption via the oral route is dependent upon the status of the pH of the GIT. The peak plasma concentration of oral misoprostol is higher when taken on an empty stomach as compared to when taken with food. Since in our study most of the subjects were on liquid diet during the process of induction, we have assumed that the misoprostol was absorbed well and almost equally in all subjects.

Therefore, the higher peak plasma concentration achieved by the oral route when coupled with frequent repeated doses (2^{nd} hourly) results in a sustained plasma level of misoprostol acid and this concentration is higher than that of the vaginal tablets. This leads to uterine contractions of adequate strength and frequency. This is displayed through the clinical effects of a shorter interval between induction and active labour and henceforth and a shorter induction to delivery interval as is found in our study.

Looking at the NICU admissions, as represented in table 18, the results of both the groups weren't statistically significant. There were a total of 7(14%) NICU

admissions in the oral group, out of which 1(2%) was admitted in view of respiratory distress. 3 (6%) went to NICU in view of low birth weight and 3 (6%) went to the Kangaroo mother care ward. Similarly 2 (4.3%) went to the NICU in view of respiratory distress, 1 (2.2%) in view of LBW and 2 (4.3%) went the KMC ward; in the vaginal group. Similar results in conjunction with our study were seen with the trial conducted by Sharma DD et al, they too found that the NICU admissions in both the groups were comparable (oral- 9, vaginal-4) and this was of no statistical significance[30]. Corresponding to this finding of ours, Jindal Promila et al had found in their study that the oral and vaginal groups had statistically insignificant difference with regard to the neonatal outcomes (NICU admissions – oral had 2 , vaginal had 0)[15]. Roxane C et al had also found similar results. They saw that there were 7(5.7%) unplanned NICU admissions in the oral group and 8(5.8%) in the vaginal group. They concluded that they found no statistically significant difference in the neonatal outcomes between the two groups[13].Out of the 7 (14%) babies who went to the NICU in the oral group, 1 was admitted in view fetal distress (uterine hypertonus was documented in the mother) while out of the 9(10.8%) babies born to the women from the vaginal group, went to the NICU, 2 had respiratory distress; (of which uterine hypertonus was observed in the patient, 1 had thick MSL with a pathological CTG trace). Total 3(6%) babies in the oral group and 2(4.3%) babies in the vaginal group were admitted in the KMC ward. Data was again statistically insignificant.

In the present study, except induction to delivery time and induction to onset of active labour both of which were shorter in the oral group, none of the other variables were statistically different between the two groups.

CONCLUSION

The present study compared the oral route of administration of misoprostol in the dose 25 mcg, 2nd hourly and the vaginal route of administration of misoprostol in the dose 25 mcg, 4th hourly, for IOL in patients presenting with PROM at term gestation. The results of the present study showed that orally administered misoprostol results in a shorter induction to active labor interval and a shorter interval between induction and delivery, as compared to vaginally administered misoprostol, with similar rates of side effects experienced and similar incidence of augmentation required with oxytocin, in both the routes of administration.

Oral misoprostol as an inducing agent is a simpler, effective and more convenient route of administration for the patients. However, our results need validation from adequately powered, well designed large scale randomized trials.

SUMMARY

The present one year RCT was conducted from 1st January 2018 to 31st December 2018 in the labour room of KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi.

According to the WHO guidelines, induction of labor should be started within 24 hours in women presenting with PROM.[4] However, there still remains room for debate over the most preferred pharmacological agent and its route of administration, for the purpose of induction of labor in cases of PROM at term.

The primary objective of the study was to compare the mean interval between induction and active labor, in the two groups. Secondary outcomes were to compare between the two groups, the interval between induction and delivery and the need for oxytocin.

All the confirmed cases of PROM, who got admitted to the labour room of KLE'S Dr Prabhakar Kore Charitable Hospital attached to KAHER'S JNMC, Belagavi, fitting the inclusion criteria, after taking written informed consent, were recruited into the trial and randomized according to a computer generated randomized numbers list, into either group 1 or group 2. The pre induction cervical score was checked and documented according to the Modified Bishop's Score.

Group1 received 25mcg misoprostol, orally, 2nd hourly upto a maximum of 12 doses or until adequate contractions began or until patient reached active labour stage. Group 2 received 50mcg misoprostol, 4th hourly upto a maximum of 6 doses or until adequate contractions began or until patient reached active labour stage.

The above mentioned variables and outcomes were studied and compared.

The minimum sample size calculated was 33 subjects in each group but to raise the power of the study, we have recruited 50 cases in the oral group and 46 in the vaginal group.

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. Quantitative variables were compared using Student T test between the two groups. Qualitative variables were calculated using Chi-Square test, Fisher's exact test (2-tailed).

We found that the two groups were comparable and similar in terms of the demographic variables. Most of the women recruited in both the groups were multigravidas, in the oral group 34 (68%) and in the vaginal group 27 (59%). The maximum occurring pre induction Bishop's score and the mean duration of PV leak [oral- 7.1±2.8 hours and vaginal-6.7 ±2.9 hours)were also comparable in the two groups.

The interval between the induction and active labour was found to be shorter (4.7±2.1hours) as compared to the vaginal group (10.1±4.5hours) with a statistically significant p value of <0.0001.

The interval between induction to delivery was also found to be significantly shorter in the oral group (8.9±3.5hours) as compared with that in the vaginal group (14.1±4.4hours) with a p value of <0.0001.

The need for augmentation of labour with oxytocin was seen to be more in the primigravidas in both the groups. The primigravidas in the oral group (68%) needed more augmentation with oxytocin as compared to the vaginal group (59%).

The incidence of uterine tachysystole (oral 14%, vaginal 19.5%), uterine hypertonus (oral-2%, vaginal 2.2%) and hyperstimulation (oral- 18%, vaginal- 21.7%)

was seen more with the vaginal group but this difference did not reach statistical significance.

Oral group had 1 case of failed induction whereas there were 2 failed induction cases in the vaginal group. This data was statistically insignificant.

The rate of caesarean sections was seen to be more in the vaginal group (32.6%) as compared to the oral group (24%) and the rate of vaginal delivery was more in the oral group (68%) as compared to the vaginal group (60.9%) and these two delivery outcomes were statistically not significant.

The indications of LSCS and instrumental deliveries were also comparable between both the groups.

The neonatal outcomes were similar in both the groups with no outcome/variable reaching statistical significance. Hence the two routes were similar when analysed for neonatal outcomes.

We reached the conclusion that the oral route of administration of misoprostol has a faster rate of induction of labour in term PROM cases with a shorter interval between induction and active labour and the interval between induction and delivery, as compared to vaginally administered misoprostol.

And that the two groups are similar in terms of delivery outcomes, neonatal outcomes, need for augmentation with oxytocin, and uterine contractility side effects.

To summarize the results found in this study, the group which was administered misoprostol orally was found to have:

1. Shorter time interval between induction and active labor.
2. Shorter time interval between induction and delivery

There was no statistically significant difference between the two groups in terms of:

- Delivery outcomes (normal delivery vs. LSCS)
- Interval between active labor and delivery
- Augmentation with oxytocin
- Neonatal outcomes in terms of NICU admissions, birth weight, APGAR Score
- Number of misoprostol doses needed
- Side effects: Hypertonous, Hyperstimulation and Tachysystole

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ANNEXURE I

CONSENT FOR PARTICIPATION IN RESEARCH

Mrs. _____ we are requesting you to enroll yourself in study titled **"Oral versus vaginal administration of misoprostol, for induction of labor, in women presenting with Premature Rupture of Membranes." 1 year Randomized Controlled Trial at KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi** conducted by Dr._____, Post Graduate in M.S. Obstetrics And Gynaecology under the guidance ofDR. _____ , Professor , Department of Obstetrics And Gynaecology , KAHER'S J.N. Medical College, Belagavi.

Respected Madam we request you to participate in our study as you are eligible for participating in the study.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to participate you are free to withdraw at any time.

The purpose of research is to compare the oral versus vaginal routes of misoprostol for induction of labour in term PROM cases.

Procedur

e Involved:

If you agree to enrol yourself in my study, you will be interviewed regarding your present, past and family history, then you will be clinically examined in detail and investigated accordingly.

Risks and Benefits:

The benefits of taking part in this research are the possible shorter interval between induction and delivery and active labour.

Voluntary Participation/Withdrawal:

Taking part in the study is voluntary. You may choose not to enrol yourself in this study. Your decision will not change present or future health care services offered to you at KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality:

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely

being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation:

In the event of injury related to the study, treatment will be made available through KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi. There is no compensation or payment for such medical treatment by law. If you are injured you may contact Dr._____, at Department of Obstetrics And Gynaecology, KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi.

Questions:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr. _____, Department of Obstetrics And Gynaecology, KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi _____ or phone number: _____) or Dr _____, Professor, Dept. Of Obstetrics and Gynaecology, KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi (Ph.: _____ or phone number: _____).

If you have any queries about your rights as a study subject, you may call Dr. Roopa Bellad, Professor & Head of the Department of Paediatrics, as Chairman of KAHER's J. N. Medical College Institutional Ethics Committee on Human Subjects Research, Phone No.0831 2473777 ext-1527 at KAHER's J. N. Medical College, Belagavi.

Consent for participation in research trial

"**Oral versus vaginal administration of misoprostol, for induction of labor, in women presenting with Premature Rupture of Membranes."**

1 year Randomized Controlled Trial at KAHER'sDr. Prabhakar Kore Charitable Hospital, Belagavi

I, _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read form in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject:_____

Date :

Witness Name : _____ Signature:

Date : _____

Investigator's Name: _____ Signature:

Date : _____

Place : _____

ANNEXURE II–

ETHICAL CLEARANCE CERTIFICATE

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

Website: http://www.jnmc.edu
E-Mail : dome@jnmc.edu

Phone: (+ 91-(0)831 Office : 2471350
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ (71) **Date: 22/11/2017**

To,

Dr. Vartika Mohan,
PG student in Obstetrics and Gynaecology,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"ORAL VS VAGINAL ADMINISTRATION OF MISOPROSTOL, FOR INDUCTION OF LABOR, IN WOMEN PRESENTING WITH PREMATURE RUPTURE OF MEMBRANES 1 YEAR RANDOMIZED CONTROLLED TRIAL AT THE TEACHING HOSPITAL ATTACHED TO DR PRABHAKAR KORE CHARITABLE HOSPITAL, BELAGAVI"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

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ANNEXURE II – PROFORMA

"ORAL VS VAGINAL ADMINISTRATION OF MISOPROSTOL, FOR INDUCTION OF LABOR, IN WOMEN PRESENTING WITH PRE LABOR RUPTURE OF MEMBRANES." 1 year randomized controlled trial at KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi

- NAME:
- IP NO:
- AGE:
- SEX:
- ADDRESS:
- OCCUPATION:
- CONTACT NUMBER:
- UNREGISTERED / REGISTERED:
- IF UNREGISTERED, REFERRED FROM:

CURRENT PREGNANCY:

- OBSTETRIC SCORE: GRAVIDA PARA ABORTION LIVING ISSUE
- LMP:
- EDD:
- C-EDD:
- POG:

MODIFIED BISHOP'S SCORE (at the time of enrolment into study):

Cervical feature	**Pelvic score**			
	0	**1**	**2**	**3**
Dilatation of cervix	**<1cm**	**1-2cm**	**2-4cm**	**>4cm**
Length of cervix	**4cm**	**2-4cm**	**1-2cm**	**<1cm**
Station of presenting part	**-3cm**	**-2cm**	**-1/0cm**	**+1/+2cm**
Consistency of cervix	**Firm**	**Average**	**Soft**	
Position of cervix	**Posterior**	**Mid, ant.**		

DURATION OF P/V LEAK*:* □ 4HOURS □4-8HOURS □8-12HOURS

□12-18HOURS □24HOURS

NST: □REACTIVE □ NON REACTIVE

EVIDENCE OF CHORIOAMNIONITIS*: (*MATERNAL BODY TEMP >_100.4F / FOUL SMELLING DISCHARGE / FUNDAL TENDERNESS/ PERSISTENT ELEVATION OF FHR BASELINE >_160 bpm)

□YES □ NO

ANY EXCLUSION CRITERIA: □ YES □NO

SERIAL NUMBER ALLOTTED TO THE SUBJECT: _____

SUBJECT IS GETTING:ORAL MISOPROSTOL □

PER VAGINAL MISOPROSTOL □

	1st dose	2nd dose	3rd dose	4th dose	5th dose	6th dose	7th dose	8th dose	9th dose	10th dose	11th dose	12th dose
Time (2nd hourly)												
ORAL DOSE												
Time (2nd hourly)												
P/V DOSE												

NEED FOR AUGMENTATION WITH OXYTOCIN: □YES (DOSE) □NO

TIME TAKEN TO REACH ACTIVE LABOR: _____hours

EVIDENCE OF UTERINE COMPLICATIONS:

- TACHYSYSTOLE (>5 contractions each lasting >40 seconds in 10 minutes for two consecutive 10 min observations) □ YES □NO
- HYPERTONUS (single uterine contraction lasting >_2minutes)

  □ YES □NO
- HYPERSTIMULATION (either of two mentioned above associated with an abnormal FHR pattern) □YES □NO

INDUCTION TO DELIVERY INTERVAL: □<24HOURS □ >24HOURS

INDUCTION TO DELIVERY TIME _____ hours

INDUCTION TO ACTIVE LABOR TIME _____HOURS

FAILURE OF INDUCTION (failure to achieve cervical dilatation ≥ 4cm after induction with escalated dose of oxytocin regimen; as per institutional protocol):

□YES □NO

MODE OF DELIVERY:

- □CESAREAN SECTION (IF YES, INDICATION):
- □NORMAL DELIVERY:
- □USE OF ANY INSTRUMENTATION (IF YES, INDICATION):

DETAILS OF BABY:

- BIRTH WEIGHT:
- SEX:
- TIME of BIRTH:
- APGAR SCORE AT 1MIN
- APGAR SCORE AT 5MIN
- NICU ADMISSION: □YES □NO
- If yes, indication _____

- SIGNATURE AND NAME OF THE INVESTIGATOR:

ANNEXURE III – KEY TO MASTER CHART

DOA - DATE OF ADMISSION

REG/ - REGISTERED CASE

UR - UNREGISTERED CASE

OBS SCORE - OBSTETRIC SCORE

POG - PERIOD OF GESTATION

NST R - REACTIVE NST

NST NR- NON REACTIVE NST

E/O CHORIO- EVIDENCE OF CHORIOAMNIONITIS

P/O - PER ORALLY

P/V - PER VAGINALLY

NO OF CT- NUMBER OF CYTOTEC TABLETS (TAB MISOPROSTOL) USED

OXY – NEED FOR AUGMENTATION WITH OXYTOCIN

Y – YES

N – NO

HRS TO AL– HOURS TAKEN TO REACH ACTIVE LABOUR

TACHYSYS– TACHYSYSTOLE

HYP'TONUS–HYPERTONUS

HYP'STIMU– HYPERSTIMULATION

FAILED IOL–FAILED INDUCTION

LSCS – LWER SEGMENT CESAREAN SECTION

VD – VAGINAL DELIVERY

I – INSTRUMENTAL DELIVERY

I/D LSCS– INDICATION OF LSCS

I/D I – INDICATION OF INSTRUMENTAL DELIVERY

BW – BIRTH WEIGHT OF BABY

APGAR1– APGAR SCORE AT 1 MINUTE

APGAR5– APGAR SCORE AT 5 MINUTES

NICU ADM– NICU ADMISSION

IND – DELIVERY- INTERVAL BETWEEN INDUCTION AND DELIVERY

AL – DELIVERY- INTERVAL BETWEEN ACTIVE LABOUR AND DELIVERY