EFFECTIVENESS AND SAFETY OF LOW DOSE VAGINAL MISOPROSTOL COMPARED TO TRANS CERVICAL FOLEY CATHETER FOR CERVICAL RIPENING IN POST TERM PREGNANT WOMEN ADMITTED TO GANDI MEMORIAL HOSPITAL, ADDIS ABABA AND FELEGE HIWOT REFERRAL HOSPITAL, BAHIR DAR, ETHIOPIA, FROM JANUARY TO DECEMBER 2014.

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JIMMA, ETHIOPIA

CATHETER FOR CERVICAL RIPENING AND INDUCTION OF LABOR IN POST TERM PREGNANT WOMEN ADMITTED TO GANDI MEMORIAL HOSPITAL, ADDIS ABABA AND FELEGE HIWOT REFERRAL HOSPITAL, BAHIR DAR, ETHIOPIA, FROM JANUARY TO DECEMBER 2014.

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# ABSTRACT

**Background**: *Post term pregnancy is one of the common indications of induction of labor in contemporary obstetric practice. However, the majority of women with post term pregnancy have unfavourable cervices. Therefore, it is mandatory to achieve cervical ripening in this group of women before proceeding to labor induction. These cervical ripening methods often result in onset of labor which makes them also labor inducing agents. Among the available various cervical ripening methods Foley catheter and vaginal misoprostol are widely used in low income countries as they are relatively inexpensive, available and effective. Nevertheless, there is paucity of studies comparing the effectiveness and safety of the aforementioned methods.*

*Thus, this study compared the effectiveness and safety of low dose vaginal misoprostol with trans cervical Foley catheter for cervical ripening and induction of labor in post term pregnant women.*

**Methods**: *- The study was conducted from January to December 2014 at Gandi Memorial Hospital (GMH) and Felege Hiwot Referral Hospital (FHRH). Quasi-experimental study design was employed and 111 post term pregnant women were enrolled to each group of cervical ripening methods. Foley catheter, number 18 gauge, was inserted trans cervically and inflated with 50ml of normal saline in women of group I at FHRH. Women in group II received 25μg of misoprostol vaginally every 6hrs for a maximum of 2 doses at GMH. Oxytocin infusion began when an indication comes to picture. Results were tabulated and statistically analysed.*

**Results**: *- Baseline obstetric variables such as gestational age and parity were not statistically different in both groups. Maternal age was found to be statistically significant (28.40 Vs 26.02 yrs; P = 0.000). Change in Bishop score is marginally significant in favour of the Foley catheter group even after controlling for maternal age (5.67 Vs 5.33; P = 0.040). Vaginal delivery within 24 hours and ripening to delivery intervals were not statistically different in both groups. Rate of vaginal delivery was found to be marginally significant being higher in the Foley catheter group (84.7% Vs 72.2%; P = 0.013). When stratified for parity, the significance was in multiparous women (93.4% Vs 78.3%; P = 0.012). Need for oxytocin was significantly higher in the Foley catheter group (75.7% Vs 43.2%; P < 0.0001).*

*Indications for caesarean section were NRFHRP and failed induction, not statistical difference was seen in both groups. Uterine tachysystole with FHR abnormality (0 Vs 12.6%; P < 0.001) and abnormal FHR is significantly higher in the Misoprostol group (6.3% Vs 26.1%; P < 0.0001). More importantly 3 cases of uterine rupture with 2 intrapartal fetal loss were encountered in the misoprostol group and all were multiparous women. Both groups were not statistically different for rates of meconium stained amniotic fluid, neonatal birthweight, low APGAR scores and NICU admissions. Furthermore 3 cases and 1 case of ENND occurred in the Misoprostol and Foley catheter group respectively. There were no cases of chorioamnionitis, endomyometritis, uterine atony and maternal death in both groups.*

***Conclusion****: - Foley catheter is relatively better in ripening the cervix but with more need for oxytocin compared to misoprostol when used in post term pregnancy. Both methods have comparable effectiveness in achieving vaginal delivery within 24 hours but higher vaginal delivery rate is seen in the Foley catheter group particularly for multiparous post term pregnant women. Higher rates of tachysystole with FHR abnormality, abnormal FHR and uterine rupture encountered in the Misoprostol group. Thus, these safety issues need to be taken into account while deciding to use misoprostol as a cervical ripening agent especially for multiparous post term pregnant women. Risk of infection is negligible with both methods.*

***Recommendation****: - We recommend Foley catheter with 50ml volume inflation shoud be used for multiparous post term pregnant women. As to the nulliparous post term pregnant women, either method can be used based on individual clinical judgement. Randomized controlled trial with larger sample size focusing on change in Bishop score, cost analysis* and maternal satisfaction with the use of each cervical ripening method in post term pregnant women need to be conducted in the future.

# ACKNOWLEDGMENT

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# ABBREVIATIONS

LNMP – Last Normal Menstrual Period

WHO – World Health Organization

MDGs – Millennium Development Goals

$PGE_1$ - Prostaglandin E 1

APGAR – American Paediatrics Gross Assessment Record

NICU- Neonatal Intensive Care Unit

C/S – Caesarean Section

GA- Gestational Age

FHR- Fetal Heart Rate

NRFHRP- Non Reassuring Fetal Heart Rate Pattern

LAPG – Locally Applied Prostaglandins

FCB - Foley Catheter Balloon

FHRH – Felege Hiwot Referral Hospital

GMH – Gandi Memorial Hospital

IUFD – Intra Uterine Fetal Death

RR – Risk Ratio

CI – Confidence Interval

SD – Standard Deviation

ANC – Ante Natal Care

CRL – Crown to Rump Length

BMI – Body to Mass Index

SPSS – Statistical Package for Social Scientists

JU – Jimma University

CBE – Community Based Education

PPH – Post Partum Haemorrhage

PI – Principal Investigator

DCT – Data Collecting Team

# CHAPTER ONE

# Introduction

## 1.1 Background

Post term pregnancy is defined as a pregnancy that continues to or beyond 42 completed weeks from the first day of the last normal menstrual period (LNMP). Although some cases of post term pregnancy likely result from an inability to recall the exact date of LNMP, many cases result from a true prolongation of gestation. The reported frequency of post term pregnancy is approximately 6% (1).

Post term pregnancy has considerable risks for both the fetus and the pregnant woman. Therefore induction of labor, i.e. initiation of labour by artificial means, has been reported to prevent adverse pregnancy outcomes in this group of women (2). Unfortunately, in the majority of women with post term pregnancy, their cervix, i.e. the outlet canal at the lower end of their uterus, is not prepared for labour or is unfavourable (3). In order to make it ready for labour, various methods can be used. These can be either mechanical methods or use of drugs. These cervical ripening agents have an additional advantage in that they may also result in onset of labor (4).

Among the mechanical methods, the commonly used one is a rubber made tube which has inflatable balloon at its tip and it is known as Foley catheter. This method is preferable as it is relatively cheap, widely available, effective and stable at room temperature. It is inserted to the woman's uterine cavity through her vagina and cervix then filled with a predetermined volume of sterile fluid. This will inflate its balloon while the other end of the tube is taped under traction to the woman's inner thigh eventually resulting in dilatation of the cervix making her ready for labour (4).

The other option is using drugs to make the cervix favourable. Of these, the one used most often is misoprostol. It initiates contraction of the uterus as well as ripening of the cervix. It can be given to the woman by oral, vaginal or rectal routes. It is inexpensive, stable at room temperature, and available in more than 80 countries, making it particularly useful in resource-poor settings. WHO (World Health Organization) recognizes the crucial role of misoprostol in reproductive health and has incorporated recommendations for its use on induction of labor where appropriate facilities are available (5).

This research compared the effectiveness and safety of use of misoprostol inserted through the vagina with Foley catheter in ripening the cervix thereby resulting in labor and delivery of a newborn among women with post term pregnancy.

### 1.2 Statement of the Problem

The main goal of labor induction is to achieve vaginal delivery in a situation where the benefits of delivery outweigh the risks of continuing the pregnancy (6). Induction of labor is directly relevant to the health related Millennium Development Goals (MDGs). It has potentials for preventing maternal complications and improving pregnancy outcome (7). A policy of labour induction compared with expectant management is associated with fewer perinatal deaths and fewer Caesarean Sections (C/S) (2).This is a priority consideration in low income countries where available resources need to be judiciously utilized (7).

Post-term pregnancy is one of the common indications for induction of labour as it has been shown to reduce adverse maternal and perinatal outcomes. Unfortunately, about 92% of these women have unfavourable cervix at 42 weeks of gestation (3). Cervical status is determined using the Bishop pelvic scoring system. Induction of labour with an unfavourable cervix is associated with prolonged labour compared to spontaneous onset of labour or induction of labour with a favourable cervix. Also an increase in instrumental deliveries and a higher rate of caesarean sections are seen in unfavourable cervix (8).

To increase the success of labour induction it is essential to achieve cervical ripening in women with an unfavourable cervix. Cervical ripening implies the process of preparing the cervix by promoting dilatation and effacement. Although several methods of labor induction exist, no single agent is superior to others or universally indicated for all women undergoing labor induction (4). Misoprostol, a synthetic prostaglandin E 1(PGE$_1$) analogue and Transcervical Foley catheter are among the commonly used cervical ripening methods. Misoprostol leads to biochemical remodelling of the cervix as well as initiates uterine contraction. The recently recommended dose of vaginal misoprostol for induction of labor at term and beyond is low dose (25 microgram (μg), 6-hourly), given the increasing sensitivity of uterine receptors to misoprostol with increasing gestational age (5, 23).

The Foley catheter acts by mechanically dilating the cervix and releasing endogenous prostaglandins. These two methods are preferred as they are relatively inexpensive making them accessible in resource poor settings, stable at room temperature and easy to administer. The Foley catheter has an added advantage in that it is reversible and lacks systemic side effects (4).

Most studies that compared the safety and effectiveness of low dose vaginal misoprostol with transcervical foley catheter were limited to term pregnancies with various indications for labor induction. Majority of them report significantly shorter mean induction to vaginal delivery interval in the misoprostol group. No statistically significant differences were observed in the rates of C/S, chorioamnionitis, uterine atony, low first and fifth minute American Paediatrics Gross Assessment Record (APGAR) scores, Neonatal Intensive Care Unit (NICU) admissions and meconium stained amniotic fluids between the two groups. One of these studies reported significant improvement of the Bishop score in the misoprostol group (10, 11, 12, 13, 14).

With regard to rate of vaginal delivery, one study reported it to be significantly higher in the misoprostol group (14). However, two studies showed no statistically significant differences between the two groups (12, 16). One study showed significantly higher vaginal delivery rate at 12 and 20 hours after cervical ripening started in the misoprostol group (10). Another study also showed statistically significant vaginal delivery rate at 12 and 18 hours after cervical ripening started in the misoprostol group but the difference was no longer statistically significant at 24 and 48 hours (13).

Rate of oxytocin augmentation found out to be significantly higher in the Foley catheter group in one study (10). On the other hand a higher rate of use of oxytocin in the Foley group without reaching statistical significance was observed in two studies (12, 16).

Rates of uterine tachysystole, hypertonus and hyperstimulation as well as rates of Non Reassuring Fetal Heart Rate Patterns (NRFHRP) were found to be higher in the misoprostol group but not statistically significant in few studies (10, 13, 14). In one study

rate of uterine tachysystole was significantly higher in the misoprostol group. Although rates of uterine hypertonus and hyperstimulation were more frequent in this group, statistical significance was not reached (12). In another study rates of uterine tachysystole and hyperstimulation were significantly higher in the misoprostol group (16).

There was a significant difference in indications for C/S between the groups, with a higher rate of failed induction in the Foley group and a higher rate of dystocia in the misoprostol group in one study. With respect to women in the misoprostol group, most of them required only one dose of misoprostol in this similar study (13).

Owing to the discrepancies in the studies so far mentioned, a meta-analysis was performed comparing these two induction agents. According to this article, both induction methods had similar effectiveness in achieving vaginal delivery, and in a similar time frame. There was also no difference in the rate of chorioamnionitis, although there were only two studies that reported this outcome. However, there was a 2.8-fold increase in the rate of uterine tachysystole with the use of misoprostol, compared with the use of a transcervical Foley catheter. The study stresses that this finding may be particularly useful when inducing labour in patients at increased risk of fetal hypoxaemia, such as those with intrauterine growth restriction, oligohydramnios, post-term pregnancy, chronic disease, thrombophilia, or pre-eclampsia. In these patients with the possibility of varying degrees of placental insufficiency, the reduction in risk of tachysystole may lead to a reduced rate of caesarean delivery for nonreassuring fetal status. Therefore, this study suggested researches focusing on these high-risk populations should be performed in the future (17).

To date only one study was done that compares the effectiveness of these two methods in post-term populations with unfavourable cervix. This prospective quasi-randomized controlled trial done by M. Kandil et al. included one hundred primigravid women with post-term gestations of 41 weeks or more and a Bishop score of <4 and equally allocated into two groups. The findings reported were no cases of rupture of membranes occurred during catheter insertion; no significant difference was noted for Bishop Score at

induction, mode of delivery, abnormal uterine activity, Fetal Heart Rate (FHR) abnormality, chorio-amnionitis and APGAR score at 1 and 5 minute between the two groups. Abnormal uterine activity occurred in three cases in the misoprostol group, but none in the Foley group. FHR abnormality that required immediate C/S was noted in one case in the Foley group but three in the misoprostol group. Three cases in the misoprostol group passed thin meconium, but their FHR tracings showed no abnormality. No case required intubation or admissions to NICU, but all babies of C/S were resuscitated at the delivery room and had quite normal neonatal periods. On the other hand significantly shorter induction to delivery interval and significantly higher requirement of oxytocin augmentation in the Foley group compared to the misoprostol group. The study concluded that fluid filled Foley catheter seems to be superior to 25 μg vaginal misoprostol regimen, when used to induce labor in primigravidae with post-term gestations with the advantage of having a shorter induction delivery interval, but more need for oxytocin augmentation. None of the pregnant women included in this study reached 42 weeks of gestation (18). Although numerous studies have demonstrated the benefits of routine induction as early as the beginning of 41 weeks of gestation in reducing adverse maternal and perinatal outcomes, Still Post term pregnancy is defined as a pregnancy of 42 weeks or more of gestation. Thus by definition the pregnant women included in this study were not post term.

Therefore to the authors` knowledge, this is the first study to compare the effectiveness and safety of Trans cervical Foley catheter with low dose vaginal misoprostol on both primigravid and multigravid post term pregnant women.

**Significance of the study**

Timely labor and delivery is of paramount importance in obstetric practice. This appears to be reasonable particularly in women with post term pregnancy given the associated risks for both the fetus and the pregnant woman. So induction of labor remains the only option for this group of women. The high rate of unfavourable cervix in these women poses a challenge for successful labor induction. These can be tackled through administration of cervical ripening agents. Although several methods of cervical ripening agents exist, no one method failed to be consistently superior to the other with regard to safety and effectiveness. Thus this research with the aim of providing one solution to the inconsistencies so far created focusing on two induction methods which are applicable in low income countries as they are widely available, relatively inexpensive and effective. As there is no similar research undertaken to date, the results of these study will be a valuable reference for the clinical practice of labor induction in women with post term pregnancy not only for our country but also for other low income countries world wide. It also opens door for further research to be done on such kinds of women in the future.

# CHAPTER TWO

# Literature Review

Induction of labor is frequently implemented in modern obstetric practice with variable rates from region to region across the World. In the United States, the number of pregnant women undergoing induction of labor has more than doubled, from 9.5% in 1990 to 23% in 2009. The availability of cervical ripening and labor induction agents as well as timely indicated births by physicians is the common reason for this rising rate of labor induction (19). In the United Kingdom, about 20% of all deliveries are by induction of labor while 11.4% was reported for Latin America (20). An increased rate of induction of labor for post-term pregnancies over a 15-year period was associated with decreased stillbirth rates in Canada (21). In a systematic review by Hussain et al., it has been shown that elective induction of labor for prolonged pregnancies at or beyond 41 leads to significant reduction in perinatal mortality (22). In developing countries, the rates are generally lower, but in some settings they can be as high as those observed in developed countries (23).

One analysis performed in seven African countries found out that average rate of induction was 4.4% with the lowest being in Niger (1.4%) and highest in Algeria (6.8%). Pre-labor rupture of membranes was the commonest indication for induction of labor. Post term pregnancy accounts for an average rate of 11.5%. The number of perinatal deaths among induced post term pregnant women reduced when compared to those not induced but not statistically significant. The unmet need for induction of labor was relatively high in all countries. These low rates of induction of labor in Africa closely reflect the very high perinatal mortality rate of 56 per 1000 live births for the region according to WHO estimates, the highest in all the world regions (7).

Induction of labor however is not without its own risks. It often results in a prolonged labor and increases the rate of cesarean delivery, both of which are associated with increased maternal and neonatal morbidity (6, 8). Ripening of an unfavorable cervix has

become an integral part of the labor induction process. The best method of cervical ripening remains controversial; no one method has proved to be superior.

The Trans cervical Foley catheter is widely used method in developing countries for pre-induction cervical ripening (24). The use of Foley catheter for induction of labor was first described in 1967 by Embery and Mollison (25). Since then different sized foley catheters with different filling balloon volumes have been utilized with different success rates (10 – 18). Lately misoprostol has been discovered and found to be an effective cervical ripening method. Several studies have been performed that compared the efficacy of Trans cervical Foley catheter versus vaginal misoprostol for cervical ripening.

Lemyre M. et al. performed a randomized controlled trial to compare the efficiency of intracervical Foley catheter and vaginal misoprostol for cervical ripening. A total of 62 pregnant women requiring cervical ripening at term were randomly assigned to get an intracervical Foley catheter installed for 12 hours or to receive 25 μg of intravaginal misoprostol every 4 hours for 12 hours. Thirty-one women were randomized to each method. Compared to women in the Foley catheter group, those receiving misoprostol delivered 5.6 hours earlier (17.7h vs 23.3h p<0.003), their labor started 3.9 hours earlier (9.6h vs 13.5h p<0.01) and their Bishop score improved of 2.0 more points (5.7 vs 3.7 p<0.02). More women were delivered 12 and 20 hours after cervical ripening started (10 vs 1 p=0.003; 20 vs 9 p=0.005). Fewer of those women required oxytocin (21 vs 30 p<0.006) or amniotomy (15 vs 25 p<0.02). Both groups were similar for demographic factors. Rates of nonreassuring fetal monitoring, abnormal uterine activity, caesarean, meconial fluid and low APGAR did not differ between both groups. The authors` concluded that vaginal misoprostol is a more efficient cervical ripening method than Foley catheter (10).

A prospective randomized controlled trial to compare the safety and efficacy of a low dose intravaginal misoprostol and intracervical Foley's catheter for cervical ripening done by T.O Tabowei et al. showed failure to achieve cervical ripening within two hours was reduced with misoprostol (Relative Risk [RR] 0.63, 95% Confidence Interval [CI]

0.43 - 0.92). Need for oxytocin augmentation was less in the misoprostol group (RR 0.76, 95% CI 0.64 to 0.91). No significant differences existed in rates for uterine hyperstimulation, Caesarean section, maternal and neonatal morbidity.

Pregnant women at term requiring pre-induction cervical ripening were randomized to receive either 25 μg of intravaginal misoprostol every four hours (n = 60) or intracervical Foley's catheter (n = 61). The study concluded that intravaginal misoprostol in a low dose was compared to intracervical balloon catheter for pre-induction ripening of the cervix (12).

O.B. Moraes Filho et al. performed a randomized controlled trial comparing the effectiveness and safety of 25 μg vaginal misoprostol versus Foley catheter and oxytocin for cervical ripening and labor induction in pregnant women with unripe cervices. In this study 240 women with a term or post term pregnancy were randomly divided into the misoprostol group (n=119) and Foley catheter group (n=121). Misoprostol was more effective in inducing labor than Foley catheter and oxytocin. Mean induction-to-vaginal delivery time with misoprostol was shorter (17.3 vs. 20.2 hours, p = 0.016). There were no significant differences in uterine contraction abnormalities, puerperal infection or neonatal outcomes. Thus, vaginal misoprostol is more effective than and as safe as Foley catheter and oxytocin for induction of labor in term and post term pregnancy (13).

Another randomized clinical trial was performed by Vahid Roudsari F et al. on 108 pregnant women with Gestational Age (GA) of >37 weeks to compare low dose vaginal misoprostol (n=49) with Foley catheter(n=59) showed similar maternal and perinatal outcomes. Vaginal delivery was significantly higher in misoprostol group (89.9 vs. 62.7, p < 0.01). The mean of delivery time was significantly shorter in misoprostol group (11.08 ± 5.6 vs. 13.6 ± 16.0 h, p < 0.05). Thus, in the cases of pregnancy termination and unripe cervix, two methods of misoprostol and Foley catheter were considered suitable, but it seemed that misoprostol decreases the delivery time and was needed for the caesarean section (14).

In a randomized controlled trial by M. Kashanian et al. on 300 pregnant women with GA ≥ 28 weeks comparing low dose intravaginal misprostol(n=100) Vs Foley catheter(n=100) Vs Both combined(n=100) showed a statistically significant difference in the induction to delivery interval between the three groups being shorter in the misoprostol group.

The induction to active phase interval was also shorter in the misoprostol group without any significant difference. There were no statistically significant differences between the 3 groups regarding rate of caesarean delivery, APGAR score at 1 min and 5 min. According to the results of this study, it seems that intravaginal misoprostol alone is more effective than the other 2 methods; moreover, it seems that the combination of intravaginal misoprostol with cervical traction does not increase the success rate of misoprostol administration, and that the 2 approaches do not have a synergistic effect (11).

A prospective randomized controlled trial was conducted by Chung et al. to determine the efficacy of combination intravaginal misoprostol and intracervical Foley catheter for prelabor cervical ripening. In this study 146 pregnant women with GA ≥ 28 weeks were included and 49 of them assigned to low dose intravaginal misoprostol group, 54 of them to the Foley catheter group and 43 of them to the combination group. There was no difference in vaginal delivery rates (misoprostol, 63.3%; Foley, 57.4%; combination, 58.1%; $P$ = .81). There were also no statistically significant differences in the interval between induction to induction to delivery among the three groups. The study concluded that intravaginal misoprostol and intracervical Foley catheter are comparable for preinduction cervical ripening. The combination of the two methods did not provide additional efficacy (16).

Vaknin Z. et al. performed a systematic review and metaanalysis of publications comparing the efficacy and safety of cervical ripening and labor induction by Foley catheter balloon (FCB) Vs locally applied prostaglandins (LAPG) in the third trimester of pregnancy. LAPG had a significantly increased risk of excessive uterine activity ($P$ =

.001). FCB had a significantly higher risk of oxytocin induction/augmentation during labor ($P$ = .0002). Cervical prostaglandin-E2 was less effective ($P$ = .04), and vaginal prostaglandin-E1 bore a significantly higher risk of excessive uterine activity ($P$ < .0001) and meconium staining ($P$ = .04). Thus, FCB and LAPG result in similar caesarean delivery rates, that FCB bears a higher risk of oxytocin use for labor induction and/or augmentation, and that LAPG carries a higher risk of contraction abnormalities (26).

A systematic review by Heinemann J. et al. on weather mechanical methods of cervical ripening increase infectious morbidity or not showed that compared with the use of pharmacologic agents alone, maternal and neonatal infectious morbidity appears to be increased when mechanical agents are used for cervical ripening. Similar results were noted for patients who underwent ripening with Foley catheter alone in comparison with pharmacologic agents (27).

In a recent Cochrane review of mechanical methods for induction of labor conducted by Jozwiak M. et al. reported that mechanical methods reduced the risk of hyperstimulation with fetal heart rate changes when compared with vaginal prostaglandins: vaginal PGE2 (eight studies; 1203 women, RR 0.16; 95% CI 0.06 to 0.39) and misoprostol (3% versus 9%) (nine studies; 1615 women, RR 0.37; 95% CI 0.25 to 0.54). Risk of caesarean section between mechanical methods and prostaglandins was comparable. Serious neonatal and maternal morbidity were infrequently reported and did not differ between the groups (28).

In another review by C. Vayssie`re et al. on prolonged and post term pregnancies recommended the lowest possible dose of misoprostol, starting with a vaginal dose of 25 µg every 3–6 h, to be used for inducing labor in post term pregnant women where as placement of an intracervical Foley catheter is an effective mechanical means of inducing labor, with less uterine hyperstimulation than prostaglandins and no increase in the caesarean section rate. Nonetheless, as the risk of infection might be increased, this technique requires more robust evaluation before entering general practice (29).

Through out our literature search, we found five studies that compared Foley catheter with different sizes and balloon filling volumes and various doses of vaginal misoprostol in African countries. Two of these studies done by T.O Tabowei et al. and M. Kandil et al. were already discussed in detail in this study as they used low dose of vaginal misoprostol per the recent recommendation. The third study performed by B.B. Afolabi et al. concluded that a single 100 μg dose of intravaginal misoprostol is more efficacious than intracervical insertion of Foley catheter for cervical ripening and induction of labor.

They recommended further studies using lower doses are needed to determine the safest dose as they found more frequent uterine hyperactivity and rupture in the misoprostol group (30).The fourth study done by O.A. Adeniji et al. found out that a 50 μg intravaginal misoprostol is as effective a pre-induction cervical ripening agent as transcervical Foley catheters (31). The fifth study done by A.B. Ande et al. concluded that the sequential combination of intracervical Foley catheter and 50 μg intravaginal misoprostol for cervical ripening and induction of labor appears to be a safe and more effective method compared to intravaginal misoprostol in parturient at term with unfavourable cervices (32). Four of the above studies were done in Nigeria while one study was done in Egypt.

None of the studies mentioned above were solely performed on women with post term pregnancy. Achievement of vaginal delivery within 24 hours is a major indicator of effectiveness for these cervical ripening methods and it is not assessed in the majority of studies done so far. One of the safety issues for these cervical ripening methods is infectious morbidity which is also not well addressed in most of the studies.

Our study was conducted on post term pregnant women and we included those issues mentioned above so that effectiveness and safety of the two cervical ripening methods can be well addressed.

# CHAPTER THREE

## Objectives

### 3.1 General Objective

To compare effectiveness and safety of 25 μg of vaginal misoprostol versus Foley catheter for cervical ripening and labor induction in post term pregnant women with unfavourable cervices admitted to Gandi Memorial Hospital, Addis Ababa and Felege Hiwot Referral Hospital, Bahirdar from January to December, 2014.

### 3.2 Specific Objectives

3.2.1 To identify demographic and baseline obstetric characteristics in the Misoprostol group as   compared to the Foley catheter group.

3.2.2 To compare the achievement of vaginal delivery within a relatively acceptable short time period between the two cervical ripening methods.

3.2.3 To determine the improvement in Bishop Score after administering Misoprostol compared  to Foley catheter.

3.2.4 To measure rates of caesarean delivery, vaginal delivery, oxytocin need, abnormalities in uterine activity and fetal heart rate in the Misoprostol group as  ompared to the Foley catheter group.

3.2.5 To measure rates of maternal and neonatal complications between the two cervical ripening methods.

# CHAPTER FOUR

# Methods and Materials

## 4.1 Study Area and Period

The study was conducted at Gandi Memorial Hospital (GMH) and Felege Hiwot Referral Hospital (FHRH) from January 1, 2014 to December 31, 2014. GMH is located at Addis Ababa, Ethiopia whereas FHRH is located at Bahir Dar, about 500 kilo meters to the North of the capital city, Addis Ababa. Both are teaching hospitals whereby Medical Interns and Resident physicians do the daily clinical practice under the supervision of the senior physicians.

## 4.2 Study Design

Quasi- experimental study design was employed.

## 4.3 Population

### 4.3.1 Source population

All women found to be post term (GA of ≥42 weeks) from the first date of reliable LNMP or from obstetric ultrasound done till 20 weeks of GA. They were admitted from Antenatal Care Clinic (ANC) to Maternity ward in both hospitals.

### 4.3.2 Study population

Women with post term pregnancy that met the inclusion criteria and found to be admitted during the study period were the study population. GMH uses misoprostol for cervical ripening and induction of labor whereas FHRH uses Foley catheter. At GMH 25 µg of misoprostol, which is prepared by breaking the 200 µg tablet, is inserted every 6 hours for a maximum of 2 doses to the posterior vaginal fornix using a digital vaginal exam on the date of admission.

Intravenous oxytocin infusion is started 6 hours after the last dose of misoprostol in those with no labor onset. A woman in whom labor begins after misoprostol insertion, Oxytocin is used if latent phase of labor is prolonged (> 8hrs) or active phase of labor abnormality encountered in the presence of inadequate uterine contractions. On the other

hand at FHRH after a sterile speculum is inserted and the anterior lip of the cervix is grasped with a tenaculum, ring forceps is used to push the distal end of number 18 gauge Foley catheter through the cervix into the extra-amniotic space. It is then inflated with 50 ml of sterile saline and pulled back snugly against the internal os and taped to the inner aspect of thigh with minimum traction. Catheter is left in place till expelled spontaneously, otherwise it is removed 12 hours after insertion. Once the catheter is extruded and no labor by then, intravenous oxytocin infusion is initiated. Both hospitals use the protocol prepared by the Federal Ministry of Health (FMOH) of Ethiopia for induction or augmentation of labor using oxytocin. According to the protocol 2 International Unit (IU) of oxytocin is added to 1000 ml of Normal saline or Ringers lactate. The number of drops is increased every 30 minutes starting from 20 drops/min (2 milli International Unit per minute (mIU/min)) till adequate uterine contraction is achieved which 3 to 5 contractions every 10 minutes each lasting more than 40 seconds or maximum dose (40mIU/min) is reached. Labor is followed using 'induction chart' that includes date, time (every 30 minute observation), oxytocin (miu in a liter, miu/ minute, drops/ minute), contractions (frequency, duration), fetal and maternal conditions, and cervical status. Once active labor is diagnosed, it is monitored using a Unit modified WHO partograph with individualized Alert Line based on cervical dilation at a gradient of 1 cm/h and Action Line 2 h to the right of the Alert Line. Intermittent FHR monitoring using pinnard fetoscope and uterine activity monitoring is done during labor follow up. If abnormal uterine activity is detected, the patient is turned to her left side; oxygen inhalation started and oxytocin infusion is discontinued. If it is corrected with these management and both the mother and fetus are in a good condition, the oxytocin infusion is re-started at half dose of the last dose. Amniotomy is performed when feasible. Failed induction is diagnosed if there is no cervical change or fetal descent while in latent phase of labor or adequate uterine contractions are not achieved after 6 to 8 hours of oxytocin administration and use of the maximum dose for 4 to 6 hours.

### 4.3.2 a) Inclusion Criteria

1. Bishop score $\leq 4$
2. Singleton pregnancies
3. Vertex presentation
4. Normal FHRP
5. Capacious pelvis based on clinical pelvimetry

### 4.3.2 b) Exclusion Criteria

1. Intrauterine Fetal Death(IUFD)
2. Ruptured membranes
3. Previous any uterine surgery
4. Clinically detected vaginal infection
5. Estimated fetal weight $\geq 4000$gms
6. Any other obstetrical or medical complication
7. Contra-indication to prostaglandin use

## 4.4 Sample size and Sampling technique

### 4.4.1 Sample size

To calculate our sample size, we used a secondary outcome parameter from a previously published study in order to avoid having smaller sample size which will occur should a primary outcome parameter be used. We hypothesized that need for oxytocin will be reduced by 40% in the misoprostol group as compared to the Foley group. For the detection of this difference with a level of significance of 0.05 and a power of 0.8 as well as Risk Ratio (RR) of 2.0 and upper limit of Confidence Interval (CI) of 3.0, 111 patients were required in each group. The double proportion population formula as shown below was utilized to calculate our sample size.

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}}\sqrt{2\bar{P}(1-\bar{P})} - Z_\beta\sqrt{P^1(1-P^1) + P^2(1-P^2)}\right)^2}{(P^2 - P^1)^2}$$

where $P_1$ (40) and $P_2$ (80) are the expected proportions in each group, and $\dot{P}$ (60) is the simple average of the expected proportions. Variables $Z_{1-\frac{\alpha}{2}}$ and $Z_\beta$ are the standard normal Z values corresponding to the selected alpha (2-sided test) and beta, respectively.

### 4.4.2 Sampling technique

Beginning from the first date of data collection, a non-probability consecutive sampling technique was used to select the participants.

## 4.5 Variables

### 4.5.1 Independent Variables

#### 4.5.1.1 Predictor variable: Cervical ripening method (Misoprostol versus Foley Catheter)

#### 4.5.1.2 Confounding variables:

Maternal age in years,

Gestational age in weeks,

Parity (number of live and still births)

### 4.5.2 Dependent Variables

#### 4.5.2.1 Primary outcomes

Vaginal delivery rate within 24 hours (yes vs no)

Ripening to delivery interval in hrs

#### 4.5.2.2 Secondary outcomes

1. Mode of delivery (Vaginal delivery, Cesarean delivery, laparatomy)

2. Change in Bishop Score (Bishop score after administration of cervical ripening Agent minus before administration)

3. Need for oxytocin (yes vs no)

4. APGAR score of the neonate $< 7$ at $1^{st}$ – and $5^{th}$ – minute after birth (Yes vs no)

5. Abnormal uterine activity (Uterine tachysystole with or without FHR normalities)

6. Indications for caesarean section (NRFHRP, Failed induction, Dystocia)

7. NICU admission (yes versus no)

8. Endomyometritis (yes versus no)

9. Chorioamnionitis (yes versus no)

10. Uterine atony (yes versus no)

11. Uterine rupture (yes versus no)

12. Stillbirth (yes versus no)

13. Maternal death (yes versus no)

14. Early Neonatal Death (ENND) (yes versus no)

15. Placental Abruption (yes versus no)

16. Hysterectomy (yes versus no)

17. Post partum Haemorrhage (yes versus no)

## 4.6 Data Collection

### 4.6.1   Data collection tool

The demographic characteristics and clinical outcomes of interest were recorded in customized data extraction proforma designed for the study.

### 4.6.2 Data collection technique

The data was recorded by attending midwife nurse under the supervision of resident physician whose responsibility is to examine and admit post term pregnant women to the wards, follow them in labor till delivery and afterwards for the development of any complications. The obstetrician on duty will be consulted for any queries that may occur in these processes. Given the experience of these physicians practising the ripening and induction techniques for many years at both hospitals, we didn't find the necessity of performing a pre-test feasibility study.

The midwife nurses who collect the data were given a brief orientation on data extraction from patient chart as well as on inclusion/exclusion criteria. Logistic support relevant for the study was provided for the data collectors.

## 4.7 Data Quality Control

The resident physician checks 10% of the data for accuracy and completeness. Regular supervision by the resident physician and assistance if the midwife has any queries was undertaken.

## 4.8 Data Processing and Analysis

All data were summarized on master sheet after they were coded and fed to computer to make ready for analysis. After double entry into a computer database using EPiInfo, data were analyzed using statistical package for social scientists (SPSS) version 16 software. To calculate the mean difference in continuous outcome variables between the two groups, student's independent t-test was used. In the test of association between the predictor- and continuous outcome-variables, the effect of potential confounders was controlled using Generalized Linear Models. For the categorical outcome variables, risk difference was calculated for each predictor variables. Statistical association between the predictor variable and categorical outcome variables was calculated using z-test. For these variables, potential confounders were controlled by running a binary logistic regression model. Mean differences and tests of association have 95% Confidence Intervals as an indicator of statistical significance and precision. A P value ≤ 0.05 is a cut-point for to determine the statistical significance of the tests. Values less than or equal to 0.05 were considered statistically significant.

## 4.9 Ethical Consideration

Official letter was obtained from Jimma University (JU) Research and Graduate studies coordinating office and submitted to the responsible authorities of both hospitals to have permission for data collection.

Although safety of each induction methods is a matter of concern that was addressed with this study, these methods are already being practiced in these hospitals and no new intervention was done to the subjects under study. However, all participants were told

about the study and a written informed consent was obtained once they agreed to be involved in the study.

## 4.11 Dissemination Plan

The final results of this study will be submitted to the advisors, JU research, graduate studies and CBE coordinating office and to publishers for possible evaluation and publication of the paper. A valuable recommendation was made based on the result obtained at the end of the study that is going to be implemented during the clinical practice in these segments of the population throughout the country.

## 4.12 Operational Definitions

**Gestational age**: it is the duration of pregnancy from the first date of LNMP or from ultrasound scan performed till 20 weeks of gestation.

**Parity**: is the experience of giving birth, be it alive or dead, after 28 completed weeks of gestation. Nulliparous woman is the one who didn`t have birth before whereas multiparous woman has given one or more birth.

Bishop score: is a method used to assess favorability of cervix based on cervical consistency, dilatation, effacement, position as well station of the presenting part. Each component is assigned a score ranging from 0 to 3 and the composite score is interpreted as follows:

$\leq 4$ is unfavourable cervix

5 to 8 is intermediate and

$\geq 9$ is favourable cervix.

**Cervical ripening methods**: are agents used to facilitate favorability of the cervix. E.g. misoprostol, Foley catheter Labor induction methods: are agents used to initiate labor. E.g oxytocin, Misoprostol, Foley catheter Labor augmentation methods: are agents used to strengthen spontaneously nitiated labor. E.g Oxytocin.

**Ripening to delivery interval**: is the time from insertion of a particular cervical ripening method to the vaginal delivery of the fetus.

**Cesarean delivery**: is delivery of a viable fetus ($\geq$28 weeks) through an incision in the abdominal wall (laparatomy) and the uterus (hysterotomy).

**Chorioamnionitis**: is infection of the chorioamniotic membranes manifesting clinically as- maternal temperature ≥ 38°c, uterinetendernes, foul smelling amniotic fluid through the vagina, maternal or fetal tachycardia or Increased white blood cell count.

**NRFHRP**: is a complex of signs showing response of the fetus to inadequate oxygenation. It can be either of the following:

      - Repetitive decelerations (variable / late)
      - Loss of beat – to –beat variability
      - Baseline bradycardia or tachycardia

Failed induction: It is diagnosed if there has been no cervical change or descent of the Presenting part or adequate uterine contraction not achieved after 6 to 8 hours of oxytocin administration.

Dystocia: literally means difficult labor and is characterized by abnormally slow labor progress.

Uterine tachysystole: six or more uterine contractions in 10-minutes, averaged over a 30- minute window. It should always be qualified as to the presence or absence of associated FHR abnormality.

**APGAR score**: is a clinical tool to identify those neonates who require rescusitation as well as to assess the effectiveness of any rescusitative measures. It is composed of five characteristics- heart rate, respiratory effort, muscle tone, reflex irritability and color. Each is assessed and assigned a value of 0 to 2.

The total score, based on the sum of the five components, is determined 1 and 5 minutes after delivery.

1-minute APGAR score: reflects the need for immediate resuscitation.

5-minute APGAR score: is a useful index of the effectiveness of resuscitative efforts.

Uterine Atony: failure of the uterus to contract properly following delivery of the fetus and placenta.

Endomyometritis: infection of the endometrium and myometrium following delivery of the Fetus and placenta.

Uterine rupture: is separation of layers of uterine wall.

Stillbirth: the absence of signs of life at or after birth.

Early neonatal death: death of a liveborn neonate during the first 7 days after birth.

# CHAPTER FIVE

## Result

A total of 235 post term pregnant women admitted to both hospitals during the study period. Of these 13 were excluded from the study as 8 of them had big babies, 4 had previous c/s and 1 with IUFD. Among the 222 women enrolled, cervical ripening using Foley catheter made for 111 and there is difficulty during attempt of insertion for 1 patient as the closed cervix failed to admit the device. She was then given misoprostol making the total number for this group 111. Among the misoprostol group, 50 of them required only one dose of misoprostol while the rest required two doses of misoprostol. Among the Foley group, rupture of membranes during insertion encountered in 2 cases. The Foley is removed after 12 hours of insertion in 51 cases while in the rest expelled by itself.

Both groups were similar in terms baseline obstetric characteristics such as parity and gestational age. There were a total of 112 nullipara and of these 50 of them were in the Foley catheter group. Out of the 110 multipara, 61 were in the Foley catheter group. Maternal age was found to be statistically significant (Table 1).

Table 1. Demographic and baseline obstetric characteristics of post term pregnant women admitted to Gandi Memorial Hospital, Addis Ababa and Felege Hiwot Referral Hospital, Bahirdar, Ethiopia from January to December, 2014 by cervical ripening method.

| Characteristic | Mean (Percent) | | Mean (Risk) Difference | 95% CI | P-value |
|---|---|---|---|---|---|
| | Group I (111)[+] | Group II (111)* | | | |
| Maternal Age (yrs), mean | 28.40 | 26.02 | 2.38 | 1.08, 3.68 | 0.000 |
| Gestational Age (wks) ,mean | 42.49 | 42.42 | 0.07 | -0.04, 0.18 | 0.096 |
| Nulliparous, n (%) | 44.6% | 55.4% | 10.8% | -23.9%, 4.1% | 0.071 |

[+]Foley catheter group      *Misoprostol group

Table 2 shows profile of labor and delivery in both groups. Change in Bishop Score is of marginal statistical significance in favour of the Foley catheter group. No difference is seen regarding ripening to active phase of labor and ripening to delivery intervals in both groups. Oxytocin need and vaginal delivery rate were found to be significantly higher in the Foley catheter group. In the Misoprostol group, there were 78 (72.2%) cases and 30 (27.8%) cases of vaginal and caesarean deliveries. The remaining 3 cases were complicated by uterine rupture. All of them were multiparous women and had tachysystol with FHR abnormality. Two doses of misoprostol inserted for two cases and one of the two required oxytocin. Both had intrapartal fetal death. For the third case, one dose of misoprostol inserted and she required oxytocin. Her newborn is salvaged. In the Foley catheter group, there were 94 (84.7%) cases and 17 (15.3%) cases of vaginal and caesarean deliveries respectively. Even though parity is not a confounding variable, we stratified rate of vaginal deliveries by parity in both groups. It showed vaginal delivery rate is higher in both nullipara and multipara in the Foley catheter group but it was significant only in multipara. Indication for caesarean section was NRFHRP for 6 (35.3%) cases and failed induction for 11 (64.7%) cases in the Foley catheter group. In the Misoprostol group, NRFHRP and failed induction accounted for 20 (66.7%) cases and 10 (33.3%) cases respectively and it was not statistically significant, P value = 0.138, (Some of the figures not shown in the table).

**Table 2.** **Profile of labor and delivery of post term pregnant women admitted to GMH, Addis Ababa and FHRH, Bahirdar, Ethiopia from January to December, 2014 by cervical ripening method**.

| Variables | Mean (Percent) | | Mean (Risk) Difference | 95% CI | P-value |
|---|---|---|---|---|---|
| | Group I (111) | Group II (111) | | | |
| Change in Bishop Score (mean) | 5.67 | 5.33 | 0.34 | -0.41, 0.71 | 0.040 |
| Vaginal delivery within 24hrs, n (%) | 76 (80.0%) | 62 (79.5%) | 0.5 | 0.49, 2.16 | 0.269 |
| Ripening to delivery (hrs) , mean | 20.50 | 20.36 | 0.14 | -1.43, 1.72 | 0.429 |
| Oxytocin need, n (%) | 84 (75.7%) | 48 (43.2%) | 32.5 | 0.19, 0.46 | <0.0001 |
| Vaginal delivery, n (%)<br>  Nullipara, n (%)<br>  Multipara, n (%) | 94 (84.7%)<br>37 (74.0%)<br>57 (93.4%) | 78 (72.2%)<br>42 (67.7%)<br>36 (78.3%) | 12.5<br>6.3<br>15.1 | 0.8, 24.2<br>-12.4, 24.9<br>4.1, 11.5 | 0.013<br>0.24<br>0.012 |

There were 18 cases of tachysystole in both groups. Those associated with FHR abnormality were 14. All occurred in the misoprostol group which is statistically significant. In those not associated with FHR abnormality, 3 of them occurred in the Foley catheter group. Rate of meconium stained liquor was not statistically significant between both groups. Whereas abnormal FHR was significantly higher in the misoprostol group (Table 3).

Table 3. Intrapartum complications of post term pregnant women admitted to Gandi Memorial Hospital, Addis Ababa and Felege Hiwot Referral Hospital, Bahirdar, Ethiopia from January to December, 2014  by cervical ripening method.

| Variables | Percent | | Risk Difference | 95% CI | P-value |
|---|---|---|---|---|---|
| | Group I (111) | Group II (111) | | | |
| Tachysystole with FHR abnormality, n (%) | 0 | 14 (12.6%) | -12.6 | -18.6, -3.7 | <0.001 |
| Meconium stained liquor, n (%) | 9 (8.1%) | 15 (13.5%) | -5.4 | -14.4, 3.0 | 0.101 |
| Abnormal FHR, n (%) | 7 (6.3%) | 29 (26.1%) | 19.8 | -30.1, -9.6 | <0.0001 |

Birthweight is not significantly different between both groups. The rate of NICU admissions, lower APGAR scores at the first and fifth minutes were higher in the misoprostol group but not statistically significant (Table 4). Neonatal resuscitation made for 11 (9.9%) neonates in the Foley catheter group and 17 (15.3%) neonates in the misoprostol group. Furthermore there were 3 ENND in the misoprostol group and 1 in the Foley catheter group (Not shown in the table). Other than the uterine rupture, there were no other maternal complications like uterine atony, chorioamnionitis, endometritis or maternal death.

Table 4.    Neonatal outcomes of post term pregnant women admitted to Gandi Memorial Hospital, Addis Ababa and Felege Hiwot Referral Hospital, Bahirdar, Ethiopia from January to December, 2014 by cervical ripening method.

| Variables | Mean (Percent) | | Mean (Risk) Difference | 95% CI | P-value |
| | Group I (111) | Group II (111) | | | |
|---|---|---|---|---|---|
| Birthweight (g), mean | 3150.45 | 3191.89 | -41.44 | -135.50, 52.62 | 0.193 |
| 1-min APGAR score < 7, n (%) | 11(9.9%) | 14 (12.8%)* | -2.9 | -0.32, 1.72 | 0.158 |
| 5-min APGAR score<7, n (%) | 1 (0.9%) | 3 (2.75%)* | -1.85 | -0.03, 3.10 | 0.138 |
| NICU admission, n (%) | 1 (0.9%) | 7 (6.4%)* | -5.4 | -15.0, 4.2 | 0.116 |

* 2 cases of Intrapartal fetal deaths are excluded.

As shown in Table 5 after controlling for maternal age, it was found out that change in Bishop Score and caesarean delivery rate were marginally significant in favour of the Foley catheter group. Rate of vaginal delivery within 24 hours is not statistically different in both methods. The need for oxytocin is significantly higher in the Foley catheter group. Abnormal FHR is significantly higher in the Misoprostol group. Rate of meconium stained liquor and 1-min APGAR score < 7 were not different in both groups.

Table 5.  Main outcome variables of post term pregnant women admitted to Gandi Memorial Hospital, Addis Ababa and Felege Hiwot Referral Hospital, Bahirdar, Ethiopia from January to December, 2014 by cervical ripening method after controlling for maternal age.

| Variables | Group I (111) | | | Group II (111) |
|---|---|---|---|---|
| | B or Exp(B) | 95% CI for B or Exp(B) | P-value | Reference |
| Change in Bishop score (B) | 0.275 | 0.002, 0.547 | 0.048 | |
| Vaginal delivery within 24hrs, Exp(B) | 0.910 | 0.426, 1.947 | 0.809 | |
| Need for oxytocin, Exp(B) | 7.799 | 3.827, 15.892 | 0.000 | |
| Caesarean delivery, Exp(B) | 0.500 | 0.253, 0.987 | 0.046 | |
| Abnormal FHR, Exp(B) | 0.210 | 0.85, 0.518 | 0.001 | |
| Meconium stained liquor, Exp(B) | 0.655 | 0.271, 1.586 | 0.348 | |
| 1-min APGAR score <7, Exp(B) | 0.724 | 0.316, 1.660 | 0.446 | |

# CHAPTER SIX
## Discussion

In this study we compared Foley catheter and low dose of vaginal Misoprostol for cervical ripening and labor induction to determine their effectiveness and safety solely limited to post term pregnant woman which was not done before. Both groups were similar in terms of baseline obstetric parameters. Maternal age is significantly different. Therefore we controlled outcome variables of interest for maternal age.

Change in Bishop Score after introduction of cervical ripening methods was marginally significant in favour of the Foley catheter group. This is against the finding in study done by Lemyre M. et al, which reported significant improvement of Bishop Score in the Misoprostol group. The inflation volume of Foley catheter used in this study was 30 ml and also 3 doses of misoprostol were inserted for all patients in this group. In another one study that used large dose of Misoprostol, pre-induction Bishop Score was not statistically different in both groups. Further study with larger sample size need to be conducted in the future.

Achievement of vaginal delivery within 24 hours, which is a main indicator of effectiveness, is not statistically different in both groups even after controlling for maternal age. The same applies for ripening to vaginal delivery interval. Two previously published studies came out with a similar finding to our study regarding achievement of vaginal delivery within 24 hours. Only few studies reported no significant difference between the two cervical ripening methods concerning ripening to vaginal delivery interval. The majority favour misoprostol in shortening this interval. This might be due to higher dose of misoprostol is used in these studies.

Oxytocin need is significantly higher in the Foley catheter group even after controlling for maternal age and this goes with the finding in almost all other studies done so far. This shows the ability of Foley catheter in inducing labor by itself is somehow limited.

Vaginal delivery rate is significantly higher in the Foley catheter group in our study and after controlling for maternal age, it is marginally significant. Multipara have significantly higher vaginal delivery rates when Foley catheter is used whereas nullipara

still have higher rate but not statistically significant. Caesarean delivery rate mirrors that of vaginal delivery rate. All of the studies done so far reported comparable vaginal delivery rates between both cervical ripening methods. All of them used Foley catheter with 30ml volume inflation. Among these, one study stratified vaginal delivery rates for parity and reported no difference in nullipara as well as multipara. In this study, indications for caesarean section were failed induction and NRFHRP which are not different statistically in both groups as also reported in few other studies.

Safety parameters like tachysytole with FHR abnormality and abnormal FHR were found to be significantly higher in the misoprostol group as compared to the Foley catheter group in our study. Only two studies came out with a similar finding to ours. In the rest of the studies still rate of tachystole is higher in the misoprostol group but statistical significance was not reached. Furthermore in our study, we encountered 3 cases of uterine rupture of which two had intrapartal fetal loss in the misoprostol group. Only one study done by B.B. Afolabi et al. reported two cases of uterine rupture with misoprostol use but they used single dose of 100μg misoprostol. With regard to other parameters like meconium stained liquor, NICU admissions, low first and fifth minute APGAR scores, it is still higher in the misoprostol group but not statistically significant. This finding is similar to all studies conducted previously. Therefore, safety is a big concern with misoprostol use particularly in multiparous women.

We found three ENND in the misoprostol group and one in the Foley catheter group. No other similar study done previously reported such outcome. No case of chorioamnionitis, uterine atony or maternal death was seen in our study.

However, this study is not without limitations. The encountered limitations are:
- The study design we used is Quasi-expermental. It will be more powerful had randomized controlled trial been conducted.
- Non-blinding of clinicians to the method of labor induction may introduce some form of bias on decision of oxytocin augmentation for the Foley group and on caesarean section rate for abnormal FHR in the misoprostol group.

# CHAPTER SEVEN:  Conclusion and Recommendation

## Conclusion

1. Foley catheter is relatively better in ripening the cervix but with more need for oxytocin compared to misoprostol when used in post term pregnancy.

2. Both methods have comparable effectiveness in achieving vaginal delivery within acceptable time period but higher vaginal delivery rate is seen in the Foley catheter group particularly for multiparous post term pregnant women.

3. Higher rates of tachysystole with FHR abnormality, abnormal FHR and uterine rupture encountered in the Misoprostol group. Thus, these safety issues need to be taken into account while deciding to use misoprostol as a cervical ripening agent especially for multiparous post term pregnant women.

4. No case of chorioamnionitis or endometritis was seen in both groups. Therefore, fear of infection previously thought to occur with the use of Foley catheter should not limit clinicians in using this cervical ripening method.

## Recommendation

1. We recommend Foley catheter with 50ml volume inflation shoud be used for multiparous post term pregnant women. As to the nulliparous post term pregnant women, either method can be used based on individual clinical judgement.

2. Randomized controlled trial with larger sample size focusing on change in Bishop score, cost analysis and maternal satisfaction with the use of each cervical ripening method in post term pregnant women need to be conducted in the future.

**ANNEX I**

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# ANNEX II
## 1. PATIENT INFORMATION AND CONSENT FORM
## PART 1. INFORMATION SHEET

We are studying on the effectiveness and safety of two methods of labor induction on post term pregnancy. Your pregnancy is diagnosed to be post term. Allowing your pregnancy to continue beyond this date increases the risk of death of the fetus as shown by different studies done so far. To avert this risk it is advised to deliver the fetus in pregnant women found to be post term.

Our study aims at comparing the effectiveness and safety of Foley catheter with that of misoprostol. Both methods of labor induction are being practiced all over the world and are found to be effective in labor initiation and delivery of the fetus. Yet no one method failed to be uniformly superior over another. Besides the effectiveness and safety of the aforementioned labor induction methods were not studied in low income countries like ours to date. At the end of this study, we hope that one labor induction method, which is relatively safe and effective, will be available. This study is expected to last for one year and we intend to enrol up to 222 participants.

With your permission, we would like to include you in this study. Your participation will be from the time of admission to discharge from the hospital. The hospital where you will be admitted has been using these labor induction methods for several years. Therefore no new interventions will be implemented during your stay in the hospital and you will be provided with all available health care. We will gather all necessary data from your medical record but will not include any information relating to your personality e.g. your name or where you live.

You do not have to take part in this study; your participation is voluntary. If you decide not to take part, you will still get all the available health care from the facility. If you decide to take part and then change your mind later, you may do so, at any time, without losing any of your rights as a patient.If you agree to participate in the study, we will ask you to read and sign the consent form. Do you have any questions?

# PART 2.   CONSENT FORM

I, the undersigned, confirm that, as I give consent to participate in the study, it is with a clear understanding of the objectives and conditions of the study and with the recognition of my right to withdraw from the study if I change my mind.

I have also been assured that I can withdraw my consent at any time without penalty or loss of the benefit of treatment. The study has been explained to me in the language I understand.

Name of patient: ……………………………………………………………….

Patient's signature: ………………………………...............

Date: ……………………………………………….

Name of data collector: ……………………………………………………

Signature of the data collector: ………………………………………..

Date: ………………………………………………………..

# 1. DATA EXTRACTION PROFORMA

Designed proforma for data retrieval on comparative effectiveness and safety study of vaginal misoprostol with foley catheter for induction of labor in women with post term pregnancy admitted to Gandi Memorial Hospital, Addis Ababa, Ethiopia and Felege Hiwot Referral Hospital, Bahir dar, Ethiopia from January to December, 2014. This proforma to be filled only for post term pregnant women with a gestational age of $\geq$ 42 weeks from reliable first date of last normal menstrual period or from obstetric ultrasound taken till 20 weeks of gestation. These women should fulfill all of the inclusion criteria (Bishop Score $\leq$ 4, Singleton pregnancies, Vertex presentation, Normal FHRP and Capacious pelvis based on clinical pelvimetry) and none of the exclusion criteria (Intrauterine Fetal Death, Previous any uterine surgery, Clinically detected genital tract infection, Estimated fetal weight $\geq$ 4000gms, Any other obstetrical or medical complications and Contra-indication to prostaglandin use).

## PART I – Demographic and Baseline Obstetric Information

1. Age in years ………………        Medical Record Number ………………………
2. Date of admission……………………      Date of discharge………………………..
3. Weight (in Kg) ………………………     Height (in meters)……………………….
4. Gestational age (in weeks) on admission……………………
5. Gravidity…………   Parity (number of previous live and still births)

   ………………………………………………………………………………..
6. Bishop score on admission………………..

## PART II – Profile of labor and delivery

1. Time at which the labor inducing agent is administered (use local time as 1:00 to 12:59 day or night)…………………………..
2. Is there rupture of fetal membranes during insertion of the Foley catheter (for the Foley group only)?     Yes……………………….      No…………………
3. Is there difficulty during insertion of the Foley catheter (for the Foley group only)? Yes………………………      No…………………

*If yes to question number 3, what is done for the patient*?

    a) Misoprostol inserted (specify dose, interval and total number

       used)…………………………………………………………………………

    b) Foley catheter re tried and inserted………………………………………...

    c) Other

       (specify)………………………………………………………………………

4. How many doses of misoprostol required (for the misoprostol group only)?

    One……………………….         Two………………

Is the Foley catheter removed after 12 hours of insertion or expelled by itself (for the Foley

group only)?

    Removed after 12 hours…………….      Expelled by itself…………………..

5. What is the Bishop score after administration of the labor inducing agent?

    a) For the Foley catheter group, by the time it expelled spontaneously or when it is

       removed after 12 hours ………………………………

    b) For the misoprostol group, 6 hours after insertion of the last dose…………….

       Time at which active phase of labor is diagnosed (use local

       time)…………………………………………………

6. Mode of delivery :

    a) Is it vaginal delivery?  Yes……………      No…………….

    b) If yes to question 7a :

       I)       Time of delivery (use local time)……………………………

       II)     Is it spontaneous vaginal delivery?  Yes ………  No……….

       III)    Is it vacuum or forceps delivery?  Yes…………  No……………

    c) Is it caesarean delivery?  Yes………….    No…………………

    d) If yes to question 7c, what is the indication for caesarean section?

       I)      Failed induction……………..

       II)    Non reassuring fetal heart rate pattern………………..

       III)   Failure of the labor to progress (mention the specific labor

           abnormality)……………………………………………………………

       IV) Other (specify)…………………………………………………….

  10. Is oxytocin used?  Yes……………..    No………………..

11. If yes to question number 10, what is the maximum dose of oxytocin required?

a) First phase: 20 drops per minute (dpm)……………………

40dpm…………………..

60dpm…………………..

80dpm…………………..

b) Second phase: 50dpm………………

60dpm………………

80dpm………………

c) Third phase: 50dpm…………………

60dpm…………………

80dpm…………………

## PART III – Intrapartum complications

1. Are there six or more uterine contractions in 10 minutes, over a 30-minute window?

Yes………………        No………………

2. If yes to question number 1, is it associated with abnormal fetal heart rate (FHR) that is FHR $\geq$ 170bpm or $\leq$ 110bpm?   Yes………………        No……………..

3. If yes to question number 2, is the FHR corrected after turning the mother to her left side, giving intranasal oxygen and intravenous fluids?

Yes……………….        No………………

4. Is meconium stained liquor detected at any time during labor?

Yes…………………        No………………..

5. If yes to question number 7, is there any FHR abnormality?

Yes………………..        No………………..

6. If yes to question number 8, is the FHR corrected after turning the mother to her left side, giving intranasal oxygen and intravenous fluids?

Yes……………….        No………………..

**PART IV – Maternal and Neonatal outcomes**

1. Weight of newborn after delivery (in grams)………………………..

2. APGAR score at first minute………… and fifth minute………………

3. Is the newborn resuscitated?     Yes…………...                No…………..

4. If yes to question number 3, how is the resuscitation made?

    a) Bag and Mask Ventilation (BMV) only………………….

    b) Laryngoscope aided oropharyngeal suctioning followed by BMV……………..

    c) Suctioning after endotracheal intubation…………………..

    d) Other (specify)………………………………………………………… ….

5. Is the newborn admitted to Neonatal Intensive Care Unit (NICU)?

    Yes……………                No……………

6. Is the mother diagnosed to have chorioamnionitis that is two of the following:
   temperature $\geq 38^{o}$c, foul smelling liquor, lower abdominal tenderness, maternal
   tachycardia ($\geq$ 100bpm) or fetal tachycardia ($\geq$ 170bpm), leucocytosis ($\geq$ 14,000
   white blood cell count)?     Yes……………..                No…………….

7. Is the uterus failed to contract after delivery?   Yes………..                No…………….

8. Is there any other maternal or neonatal complications?  Yes………..                No…….

9. If yes to question number 8, what is the specific complication?

    a) Uterine rupture…………….

    b) Post partum haemorrhage (specify cause)…………………………………

    c) Hysterectomy (specify the reason)……………………………………… …

    d) Placental abruption……………………………………………………………

    e) Maternal death (specify cause)……………………………………………

    f) Stillbirth (specify cause if possible)…………………………….. ………

    g) Early Neonatal Death (specify cause if possible)……………………………

    h) Endometritis……………………………………………………………

    i) Other (specify)…………………………………………………………

    Name of data collector……………………………………………………………..

    Date of data collection…………………………………………………………..
    Signature……………………………………………….
    
    Thank you for your time!

## Bishop's Pelvic Scoring System

| Score parameter | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| Cervical dilatation (cm) | Closed | 1-2 | 3-4 | 5 or more |
| Effacement (%) | 0-30 | 40-50 | 60-70 | 80 or more |
| Station* | -3 | -2 | -1 or 0 | +1 or +2 |
| Consistency | Firm | Medium | Soft | |
| Position | Posterior | Mid position | Anterior | |

*Station is graded from -3 to +3

Interpretation of the Bishop's score:

Score ≤ 4: Unfavourable cervix

Score 5 to 8: Intermediate

Score ≥ 9: Favourable cervix

**Scoring System**

| Sign | 0 Points | 1 Point | 2 Points |
|---|---|---|---|
| Heart rate | Absent | <100 bpm | 100 bpm |
| Respiratory effort | Absent | Slow, irregular | Good, crying |
| Muscle tone | Flaccid | Some flexion of extremities | Active motion |
| Reflex irritability | No response | Grimace | Vigorous cry |
| Color | Blue, pale | Body pink, extremities blue | Completely pink |

Data from Apgar (1953)