

Overview of Termination of Second Trimester Pregnancy after Previous Cesarean Section

Samar Mohammed Abd-elwahed , Youssef Abu Alwan Al-Sayed, Walid Abdullah Abdul Salam, Walid Mohammed Etman

**Obstetrics and Gynecology Department, Faculty of Medicine, Zagazig University, Egypt.** Corresponding author: **Samar M. Abd-elwahed**, Email: <u>sm3805731@gmail.com</u>

### ABSTRACT

Second-trimester abortion is an important component of comprehensive women's health care, and women seek termination later in pregnancy for a variety of medical and social reasons. Inducing termination of pregnancy (TOP) is often considered in the second trimester due to issues like severe preeclampsia, ruptured membranes, uncontrolled hypertension, impaired renal function, and urgent management of malignancies. Women with prior cesarean sections face an increased risk of uterine rupture, necessitating thorough counseling with the patient and their relatives before proceeding with Inducing labor (IOL). Various methods of labor induction have been studied, broadly categorized as pharmacological or mechanical can be used in the second trimester. Pharmacological approaches involve prostaglandins, oxytocin, estrogens, and mifepristone. Prostaglandin E2 (dinoprostone) is FDA-approved for cervical ripening in labor induction, although it's costly and requires cold storage. Mechanical methods for labor induction include transcervical insertion of Foley's catheter, double-balloon catheter, and laminaria tents. Among these, inserting a Foley catheter into the cervical canal is common. This technique stimulates mechanical dilation and the release of prostaglandins, aiding in labor initiation. However, the optimal method of cervical ripening is still unknown. The aim of the current study to review dinoprostone and intracervical foley's catheter, for the termination of second-trimester pregnancies in women with previous cesarean deliveries.

Keywords: Dinoprostone; Intracervical Foley's Catheter; Previous Cesarean Section

# DOI: 10.48047/ecb/2023.12.si8.807

# INTRODUCTION

Second trimester is defined as the period of gestation between 13 to 28 weeks and is commonly subdivided into early ranging from 13-20 weeks and late from 20-28 weeks gestation. Induction of abortion or labor is one of the commonest procedures used for termination of pregnancy and is one of the most provocative zones of obstetrical practice. The Termination of pregnancy by induced abortion is practiced worldwide, 22 % of pregnancies (1). Second trimester abortions constitute 10–15% of all induced abortions worldwide but are responsible for two-thirds of all major abortion-related complications while the majority of the terminations, nearly 90 %, takes place in the first trimester (2).

Indications for second trimester termination of pregnancy are variable, they are usually performed for Anticipated benefits to the mother, such as improving a medical condition which is caused or aggravated by pregnancy, including pre-eclampsia, placental abruption and certain respiratory, hepatic and cardiac disorders; or any other medical disorder affect the mother health. However, congenital fetal malformations, which are incompatible with life also constitute a major indicator for pregnancy termination (3).

Essentially pregnancy termination in cases with prior cesarean delivery become an increasingly common situation facing obstetricians due to progressive increase in the rate and incidence of cesarean births, Despite several mechanical and pharmacological methods for termination of such pregnancy but the safety and efficacy of every method are the main factors governing its choice (4).

Pharmacological ripening agents include oxytocin, misoprostol, and prostaglandins delivered orally or vaginally (5). Due to the rapidity and ease of removal when active labour is established, the controlled released inoprostone insert has become the preferred vehicle for delivering prostaglandin E2 (6).

Prostaglandin  $E_2$ , also known as dinoprostone, is the only prostaglandin approved by the US Food and Drug Administration (FDA) for cervical ripening in labour induction (7). The main advantages of prostaglandinsfor medical termination were a much shorter induction abortion interval and decreased risk of severe complications. Although vaginal prostaglandins (e.g.,Dinoprostone (PGE2, prostin E2)) are useful for cervical ripening, their efficacy is dosedependent: higher dose regimens result in increased side effects, uterine contractions and labour induction (8).

Foley's catheter placement is used for mechanical cervical ripening and stimulating endogenous release of prostaglandins and cytokines that make the cervix inducible and eases the process of termination (9). The catheter slowly dilates the cervix by introducing a small amount of fluid into the extra-amniotic space. The insertion of a Foley catheter into the cervical canal is one of the more commonly used mechanical methods and its use dates back to the 1960s (5). The technique is more cost-effective compared with other mechanical methods, and the balloon is inflated with 30–80 ml of sterile saline (10).

Mechanical methods are used to dilate the cervix, but may also increaseprostaglandin and/or oxytocin release by causing localized inflammation, while prostaglandin preparations act to promote both cervical remodeling and uterine activity (11).

### I. Intracervical Foley's Catheter in Termination of Second Trimester Pregnancy

Foley catheter with a 30 ml balloon is inserted into the intracervical canal past the internal OS and inflated with 30 ml of sterile water. The catheter is drawn to the inside of the knee and taped in place to produce a small degree of traction. Continuous fetal heart rate monitoring is performed for a minimum of 45 minutes, and the patient is transferred to the antepartum ward. After one day, a pelvic examination is performed to confirm its position in the endocervix, traction is reapplied, and the patient is allowed further time for cervical ripening. Induction commenced once the catheter fell out spontaneously (12).

# Mechanism of intracervical Foley's catheter in Induction of abortion

Induction of abortion in patients with Previous Cesarean Section had an amplified risk of rupture uterus. It should be decided after comprehensive counseling and management. Many methods have been used for labour induction, mainly including pharmacologic options or mechanical devices. However, the optimal method of cervical ripening is still unknown. Commonly used mechanical options include the standard Foley urinary catheter and specifically designed double-balloon catheter (13).

The catheter slowly dilates the cervix by introducing a small amount of fluid into the extra-amniotic space. The insertion of a Foley catheter into the cervical canal is one of the more commonly used mechanical methods and its use dates back to the 1960s. The technique is more cost-effective compared with other mechanical methods, and the balloon is inflated with 30–80 ml of sterile saline. However, most double-balloon catheters are filled with 80 ml

in the uterine balloon and 80 ml in the vaginal balloon, making it easier to quantify the technique for comparison with other methods (14).

The insertion of a Foley catheter into the cervical canal is one of the more commonly used mechanical methods. The technique was first described for the induction of labour in 1967, and is more cost-effective compared with other mechanical methods. Pharmacological methods include the use of prostaglandins, oxytocin, estrogens, and mifepristone. Prostaglandins, which are cyclopentane derivatives of arachadonic acid, are widely used in obstetrics and gynaecology. Prostaglandin E2, also known as dinoprostone, is the only prostaglandin approved by the US Food and Drug Administration (FDA) for cervical ripening in labour induction; However, dinoprostone is expensive and requires cold storage. Misoprostol, a prostaglandin E1 analogue approved for treating gastric ulcers caused by non-steroidal anti-inflammatory drugs, is often used as an off-label drug for inducing labour (6).

The unripe cervix is a major impediment to the success of labour induction and vaginal delivery. To maximise the success rate, various ripening methods are available, including mechanical devices and pharmacological options. A mechanical device was first described with laminaria tents; more recently, the standard Foley urinary catheter, as well as a specifically designed double-balloon catheter, has also been used successfully. The catheter is introduced through the cervical canal to reach the extra-amniotic space and then inflated to modify the cervical status and to keep the catheter in place. Regarding pharmacological methods, prostaglandin E2 (PGE2) administered intracervically or intravaginally has been demonstrated to be an effective ripening agent (**12**).

The effectiveness of misoprostol in cervical ripening has been demonstrated, but several case reports have suggested that the rate of serious complications, such as excessive uterine contractions and rupture, may be increased compared with other methods. In addition, there are a variety ways to administer misoprostol that include oral, vaginal, sublingual, or buccal routes, although the latter two routes are not currently recommended for labour induction (15).

Worldwide, caesarean birth is common. In Australia in 2007, almost 31% of women gave birth by caesarean section, with similar figures reported from the United States . While the overall rate of caesarean section is lower in the United Kingdom, accounting for approximately 25% of all births, rates of almost 50% have been reported in some private hospitals in Argentina, Brazil and Chile (5).

Existing data suggests non-inferiority of single-balloon catheter versus PGE2 with regards to mode of birth and induction to delivery interval. In our hospital's setting, inpatient balloon catheter is used when PGE2 is considered unsafe for cervical ripening e.g. previous Caesarean Section, but only medical staff are trained in its insertion, and inpatient PGE2 remains the standard cervical ripening method due to ease of administration for both midwifery and medical staff. Outpatient PGE2 is not used due to concerns about safety, particularly hyperstimulation (16).

We therefore aimed to investigate the use of Foley (single balloon) catheter for outpatient cervical preparation for its likely safety for outpatient use given low rates of excessive uterine activity, and potential resource and patient benefits of outpatient IOL. We were not aware of prior published research directly comparing outpatient catheter with inpatient PGE2 gel. We undertook a randomised trial to determine the feasibility, clinical effectiveness and acceptability to women of using intracervical Foley catheter in an outpatient setting vs. intravaginal Prostaglandin E2 (Prostin) gel in an inpatient setting for induction of labour (IOL) (17).

An uncommon, but potentially life-threatening complication for both the woman and her infant associated with vaginal birth, is that of uterine scar rupture (where the previous caesarean scar breaks down). Uterine scar rupture is associated with a significant risk of maternal morbidity, such as hysterectomy, genitourinary tract injury, postpartum blood transfusions, and maternal death. Increased infant morbidity and perinatal death have been reported. Uterine rupture is reported to occur more commonly after induction of labour, compared with spontaneous labour in women who have had a previous caesarean birth (17).

### II. Using Prostaglandins Especially Dinoprostone for Abortion

The procedures mainly used are extra- or intra-amniotic administration of solutions such as hypertonic saline, ethacridine lactate, PGF2 alpha and PGE2. In comparison with these procedures, the use of prostaglandin analogues may offer important advantages, the most important one being the possibility of using non-invasive routes of administration (18).

The continuous development of new analogues has now resulted in compounds that are highly effective in stimulating uterine contractility and are associated with a low frequency of side-effects; these compounds are suitable for both vaginal and intramuscular administration and are applicable for termination of pregnancy during both the early and late parts of the second trimester. The most widely used method for termination of first trimester pregnancy is vacuum aspiration. It is a highly effective procedure and the overall complication rate is low. One problem with vacuum aspiration is the mechanical dilatation of the cervical canal which is necessary from at least the 8th week and onwards.Pretreatment with laminaria tents or with prostaglandin analogues eliminates or reduces the need for mechanical dilatation and significantly facilitates the procedure. Pretreatment with prostaglandin analogues also reduces the risk of both operative and postoperative complications (**18**).

Induction of labour for intrauterine death is indicated not only for psychological reasons but also on medical grounds because the risk of coagulopathy increases if labour is delayed. Induction of labour in these patients can be difficult when the cervix is unripe. Prostaglandin analogues are commonly used nowadays for the induction with intrauterine death (19).

The success rates range from 67 to 100%. Misoprostol is probably the most preferred drug because of its low cost, stability in room temperature and ease of administration. The vaginal administration of misoprostol has been shown to be more effective compared with the oral route in the context of medical management of first- and second-trimester abortion. Most of the published regimens have recommended the intra-vaginal route (**20**).

The prostaglandins also offer a possibility as a non-surgical procedure for termination of very early pregnancy .both vaginal and intramuscular administration of the latest generation of PG analogues have been shown in several studies to be equally as effective as vacuum aspiration if the treatment is restricted to the first three weeks following the first missed menstrual period. Gastrointestinal side-effects are still a problem although of significantly less importance than if natural prostaglandins are used. Preliminary studies in which one of these PGE analogues was administered by the vaginal route indicate that selfadministration at home starts to be a reality in selected patients (**21**).

Recently proposed techniques for the termination of 2nd trimester missed abortion based on administration of the natural prostaglandins (PGs) E2 and F2 alpha or analogs derived from the parent compounds are described. With few exceptions the techniques are still experimental because of the number of cases treated remains small or because the preparations are not available for clinical use. Interpretation of reported results is often difficult because of incomplete description of procedures and pooling of missed abortion and missed labor. Because of troublesome side effects after systemic administration of natural PGs, the present tendency is to favor local administration or to use synthetic analogs that have a longer half-life and greater uterotonic potency (22).

Choice of a PG compound depends largely on availability, whereas the route of administration is determined by expertise and available facilities. Among the recently proposed PG techniques, repeated application of intravaginal PGE2 pessaries has yielded reported success rates higher than 95% with no serious complications reported but frequent unpleasant side effects. The gastrointestinal (GI) symptoms may be alleviated by preabortion cervical priming and use of antiemetic and antidiarrheal drugs. Extra amniotic administration of natural PGs appears to be highly effective for termination of missed abortion without production of side effects. Application of PG-gel is simpler than continuous infusion; the use of an indwelling catheter probably accelerates the effect. Serial intramuscular 15-me-PGF2 alpha is also highly effective (23).

The frequency and intensity of associated GI side effects can be reduced to tolerable levels by using antiemetic and antidiarrheal drugs or reducing dosages. Intravenous or intramuscular administration of the utero-selective PG analog sulprostin is acceptable because of the lack of side effects and high success rate. Cervical priming before the procedure is started has been found to shorten the induction-abortion time and to improve the success rate when natural PGs and analogs are used to terminate fetal demise (23).

#### Use of prostaglandins with scarred uterus

Termination of pregnancy with a previous uterine scar is always challenged. No matter what method is used, there are higher risks of uterine rupture than in those women without a scar. The risk of scar rupture at the time of medical termination in the presence of previous uterine scars varies from 3.8%67 to 4.3%.68 This compares to a rupture rate of 0.2% in patients with an intact uterus.69 Uterine scar rupture has been reported in both gemeprost and misoprostol regimens. No well-controlled study has shown that any method is better than the others. A small study has shown the efficacy of misoprostol in second-trimester termination in a scarred uterus. There are not enough data to show that misoprostol is safe, but at least it may be an alternative. With the rising Caesarean section rate, there will be an increasing number of women undergoing termination of pregnancy with a previous uterine scar. Current evidence would suggest that they are at an increased risk of scar rupture. Women should be appropriately counselled about the risks and consequences. The optimum chance for successful outcome is provided by the informed and alert clinician who appreciates the potential risks of the procedure and who is prepared to deal with those risks (24).

#### Dinoprostone using in induction of abortion

Prostaglandin E2 (PGE2), also known by the name dinoprostone, is a naturally occurring compound involved in promoting labor, though it is also present in the inflammatory pathway. Prostaglandin E2 is FDA approved for cervical ripening for the induction of labor in patients for which there is a medical indication for induction. When used as a vaginal suppository, it is indicated as an abortifacient from gestational week 12 to 20 or for the evacuation of uterine contents for the management of missed abortion and intrauterine fetal death up to 28 weeks. Prostaglandin E2 is also useful for the management of gestational trophoblastic disease. Importantly, it is not a feticidal agent. Given its oxytocic properties, the administration of dinoprostone should only be at the proper dosages by experienced clinicians(**24**).

While the exact mechanism of action is unknown, prostaglandin E2 causes contractions in the myometrium via direct stimulation. It binds to G protein-coupled receptors (GPCRs) EP1-4 that lead to a variety of downstream events depending on the EP subtype and cell-type-specific expression patterns. For example, EP receptors in the myometrium act via cell membrane calcium channels and intracellular cyclic 3'5'-adenosine monophosphate (cAMP). As some of the known receptors for prostaglandin E2 antagonize each other, researchers have hypothesized that the expression of these receptors determines the specific effects. The efficacy of prostaglandin E2 during pregnancy may link to the expression of these receptors. Prostaglandin E2 also promotes cervical dilation, effacement, and softening, similar to the natural progression of pregnancy, possibly due to increased collagenase secretion (22).

The role of prostaglandin E2 in inflammation is complex; it has demonstrated proinflammatory activity in specific settings and plays an anti-inflammatory role in others. These diverse functions appear to depend on the cell type and expression patterns of various receptors. It can promote the activation of inflammatory Th17 cells but suppress IL-2 and IL-12 production in other T cell subsets. Importantly, though in vitro experiments have demonstrated that prostaglandin E2 can inhibit T-cell production, in vivo studies have not yet shown similar results (**26**).

PGE2 is administered vaginally as a suppository, gel, or insert. The vaginal suppository is for the evacuation of uterine contents. One 20 mg suppository is inserted into the posterior fornix of the vagina every three hours until abortion occurs. If the abortion does not occur within twenty-four hours, or if there are severe side effects, the clinician should stop the drug. The endocervical gel and vaginal inserts are agents for cervical ripening induction. The cervical gel has a more rapid release than the vaginal insert but might be less convenient, as the procedure requires more vaginal examinations.PGE2 is inserted into the posterior fornix and replaced every six hours until labor induction, as determined by regular, painful contractions. However, drug administration should cease if there are no contractions within twenty-four hours or if there are severe adverse effects, including membrane rupture or uterine hyperstimulation (27).

The most common side effects of prostaglandin E2 concern its impact on gastrointestinal smooth muscle. The suppository correlates with the most severe side effects, with two-thirds of patients experiencing vomiting, two-fifths experiencing diarrhea, and one-third experiencing nausea. Other adverse effects include temperature elevation in half of the patients, headache in one-tenth, and shivering and chills in one-tenth. Anti-emetics and anti-diarrheal medications may be necessary before and during the drug administration to counteract these side effects (28).

The insert and gel have a less than one percent incidence of gastrointestinal symptoms. However, studies have shown that they have links to a higher chance of uterine hyperstimulation with and without fetal distress (greater than 2%) versus placebo (under1%). Additionally, they also have an increased chance of fetal distress without uterine hyperstimulation (over 2%) versus placebo (1%). There were also associated fetal heart rate changes, with and without distress. In all of these cases, removal of the product resulted in a return to normal, though one case did require treatment with tocolytics (**29**).

Prostaglandin E2 is contraindicated in patients with a known hypersensitivity to prostaglandins. As an oxytocic agent, prostaglandin E2 should be avoided in scenarios in which vaginal delivery or the induction of labor is contraindicated and should be stopped before administering oxytocin (**30**).

Clinicians should avoid the suppository should in patients with acute inflammatory pelvic disease, as well as patients with active cardiac, renal, pulmonary, or hepatic disease.

Additionally, it requires caution in patients with a history of these diseases and patients with a history of cervical malignancy, asthma, hypo- or hypertension, anemia, jaundice, pulmonary disease, or epilepsy. The prostaglandin E2 suppository is not indicated for uterine evacuation for fetuses at the stage of viability (**30**).

The gel or insert versions used for cervical ripening are contraindicated in patients with fetal distress where delivery is not imminent or who have vaginal bleeding during pregnancy, marked cephalopelvic disproportion, and/or multipara with six or more previous term pregnancies. Prostaglandin E2 should also be avoided when prolonged uterine contraction may pose a risk to uterine integrity or fetal safety, such as with prior cesarean section or major uterine surgery. Prostaglandin E2 for labor induction should also be avoided in patients with a history of asthma, glaucoma, or heart disease (**31**).

### **CONCLUSION:**

Induction of labour is a common obstetric intervention worldwide Both surgical and modern medical methods are safe and effective when provided by a trained, experienced provider.

Cervical ripening with a Foley catheter has several advantages over pharmacological methods. Therefore, we considered the Intracervical Foley's catheter method as a viable option for terminating second-trimester pregnancies in women with scarred uteri due to previous cesarean deliveries. It showed a higher percentage of complete uterine evacuations, indicating potential efficacy in this patient population.

Its recommended direction for future research to explore additional factors, such as patient satisfaction, cost-effectiveness, and long-term outcomes, to form a more comprehensive understanding of the overall benefits and risks associated with the Dinoprostone and Intracervical Foley's catheter methods. Its recommended holistic approach would aid healthcare providers in making well-informed decisions and improving the quality of care for women undergoing second-trimester pregnancy terminations in the context of previous cesarean deliveries and scarred uteri.

# No conflict of interest.

# **REFERENCES:**

- 1- Carlsson, I., Breding, K., & Larsson, P. G. (2018). Complications related to induced abortion: a combined retrospective and longitudinal follow-up study. BMC Women's Health, 18(1), 158.
- 2- Tesfaye, B., Tewabe, M., Ferede, A., & Dawson, A. (2020). Induced Second Trimester Abortion and Associated Factors at Debre Markos Referral Hospital: Cross-Sectional Study. Women's health (London, England), 16, 1745506520929546-1745506520929546.
- 3- Desouky, E., El feky, A., & Elsayed, A. A. A. A. (2021). Randomized Controlled Trial Between Vaginal Misoprostol Alone Versus Weighted Intrauterine Foley's Catheter and Vaginal Misoprostol in Termination of Mid-Trimester Abortion. Evidence Based Women's Health Journal, 11(2), 141-145.
- 4- Barakat, R. I. (2020). Different methods of termination of second trimester pregnancy with scarred uterus at Mansoura University Hospitals. The Egyptian Journal of Fertility of Sterility, 24(2), 27-34.

- 5- Chen, W., Xue, J., Peprah, M. K., Wen, S. W., Walker, M., Gao, Y., et al. (2016). A systematic review and network meta-analysis comparing the use of Foley catheters, misoprostol, and dinoprostone for cervical ripening in the induction of labour. Bjog, 123(3), 346-354.
- 6- Liu, Y.-R., Pu, C.-X., Wang, X.-Y., & Wang, X.-Y. (2019). Double-balloon catheter versus dinoprostone insert for labour induction: a meta-analysis. Archives of Gynecology and Obstetrics, 299(1), 7-12.
- 7- Church, S., Van Meter, A., & Whitfield, R. (2009). Dinoprostone compared with misoprostol for cervical ripening for induction of labor at term. J Midwifery Womens Health, 54(5), 405-411.
- 8- Makhlouf, A. M., Al-Hussaini, T. K., Habib, D. M., & Makarem, M. H. (2003). Second-trimester pregnancy termination: comparison of three different methods. J Obstet Gynaecol, 23(4), 407-411.
- 9- Saleh, H. S., El-Husseny, E. K. M., & El, K. (2020). Misoprostol only or in combination with intra cervical Foleys catheter for termination of the second trimester demise pregnancy in patient with previous caesarean sections. OGIJ Obstetrics & Gynecology International Journal, 11(6).
- Jozwiak, M., et al., Foley catheter versus vaginal prostaglandin E2 gel for induction of labour at term (PROBAAT trial): an open-label, randomised controlled trial. Lancet, 2011. 378(9809): p. 2095-103.
- **11-** Henry, A., Madan, A., Reid, R., Tracy, S. K., Austin, K., Welsh, A., et al. (2013). Outpatient Foley catheter versus inpatient prostaglandin E2 gel for induction of labour: a randomised trial. 13(1), 1-11.
- 12- Abdi, N., Alavi, A., Pakbaz, F., & Darabi, H. (2021). Vaginal misoprostol versus intracervical Foley catheter for cervical ripening in postdate primigravid women: a randomized clinical trial. BMC Pregnancy and Childbirth, 21(1), 1–6.
- 13- Pierce, S., Bakker, R., Myers, D. A., & Edwards, R. K. (2018). Clinical Insights for Cervical Ripening and Labor Induction Using Prostaglandins. AJP Reports, 8(4), e307– e314.
- 14- Yang, X., Pan, X., Li, M., Zeng, Z., Guo, Y., Chen, P., Liang, X., Chen, P., & Liu, G. (2022). Interaction between Cervical Microbiota and Host Gene Regulation in Caesarean Section Scar Diverticulum. Microbiology Spectrum, 10(4).
- 15- Tamanna Rahman, M., & Abdus Sobhan, S. (2022). Rate of Successful Induction Following Intra-Vaginal Administration of Misoprostol. Sch Int J Obstet Gynec, 5(1), 7– 13.
- 16- Gupta, J., Baev, O., Duro Gomez, J., Garabedian, C., Hellmeyer, L., Mahony, R., Maier, J., Parizek, A., Radzinsky, V., Stener Jorgensen, J., Britt Wennerholm, U., & Carlo Di Renzo, G. (2022). Mechanical methods for induction of labor. European Journal of Obstetrics and Gynecology and Reproductive Biology, 269, 138–142.
- 17- Ziadeh, H., Panel, P., Letohic, A., Canis, M., Amari, S., Gauthier, T., & Niro, J. (2020). Resection of deep-infiltrating endometriosis could be a risk factor for uterine rupture: a case series with review of the literature. F&S Reports, 1(3), 213–218.
- 18- Atuhairwe, S., Byamugisha, J., Kakaire, O., Hanson, C., Cleeve, A., Klingberg-Allvin, M., Tumwesigye, N. M., & Gemzell-Danielsson, K. (2022). Comparison of the effectiveness and safety of treatment of incomplete second trimester abortion with misoprostol provided by midwives and physicians: a randomised, controlled, equivalence trial in Uganda. The Lancet Global Health.

- 19- Glavaš, M., Gitlin-Domagalska, A., Dębowski, D., Ptaszyńska, N., Łęgowska, A., & Rolka, K. (2022). Vasopressin and Its Analogues: From Natural Hormones to Multitasking Peptides. International Journal of Molecular Sciences 2022, Vol. 23, Page 3068, 23(6), 3068.
- **20-** Queenan, J. T., Spong, C. Y., & Lockwood, C. J. (2020). Fetal Death and Stillbirth. Protocols for High-Risk Pregnancies, 397–406.
- **21-** Bhuvaneswari, K. (2020). Study on Midtrimester Termination of Pregnancy in Previous Caesarean Section: Comparison between Intracervical Foley with Misoprostol and Mifepristone with Misoprostol (Doctoral dissertation, Madras Medical College, Chennai).
- 22- Shorter, J. M., Atrio, J. M., & Schreiber, C. A. (2019). Management of early pregnancy loss, with a focus on patient centered care. Seminars in Perinatology, 43(2), 84–94.
- 23- Špoljarić, B., Svoboda, D., Gereš, D., Vince, S., Špoljarić, D., Popović, M., ... & Samardžija, M. (2020). Combination of dopamine agonist and prostaglandin administration for pregnancy termination in bitches–a novel approach. *Journal of applied animal research*, 48(1), 402-405.
- 24- Nishidhini Nagin, R. (2020). A Study of Induction of Labour with Intracervical PGE2 Gel (Doctoral dissertation, Chengalpattu Medical College and Hospital, Chengalpattu).
- 25- Franke, J. F., Oelmeier, K., Möllers, M., Möllmann, U., Braun, J., Kerschke, L., ... & Hammer, K. (2022). Termination of pregnancy in the second trimester-the course of different therapy regimens. *Journal of Perinatal Medicine*, 50(8), 1053-1060.
- 26- Konopka, C. K., Glanzner, W. G., Rigo, M. L., Rovani, M. T., Comim, F. V., Gonçalves, P. B. D., Morais, E. N., Antoniazzi, A. Q., Mello, C. F., & Cruz, I. B. M. (2015). Responsivity to PGE2 labor induction involves concomitant differential prostaglandin E receptor gene expression in cervix and myometrium. Genetics and Molecular Research : GMR, 14(3), 10877–10887.
- 27- Bakker, R., Pierce, S., & Myers, D. (2017). The role of prostaglandins E1 and E2, dinoprostone, and misoprostol in cervical ripening and the induction of labor: a mechanistic approach. Archives of Gynecology and Obstetrics, 296(2), 167–179.
- **28-** Nakanishi, M., & Rosenberg, D. W. (2013). Multifaceted roles of PGE2 in inflammation and cancer. Seminars in Immunopathology, 35(2), 123–137.
- 29- Abdelaziz, A., Mahmoud, A. A., Ellaithy, M. I., & Abees, S. H. (2018). Pre-induction cervical ripening using two different dinoprostone vaginal preparations: A randomized clinical trial of tablets and slow release retrievable insert. Taiwanese Journal of Obstetrics & Gynecology, 57(4), 560–566.
- 30- Xi, M., & Gerriets, V. (2019). Prostaglandin E2 (Dinoprostone).
- 31- Swartout, J. P., & Ramin, K. D. (2008). Controlled-release dinoprostone vaginal insert for cervical ripening and labor induction. Expert Review of Obstetrics & Gynecology, 3(1), 13-20.