# DISSCUSSION

Postmaturity is the condition of a baby that has not yet been born after 42 weeks of gestation .Post-mature births can carry risks for both the mother and the fetus [(2)] ,so post term pregnancy may be a reason to induce labor. Although there is no ideal predictor of successful induction of labor, cervical status is now accepted as the most useful clinical parameter.

Cervical ripening is an active process resembling an inflammatory reaction, among factors regulating cervical ripening; prostaglandins are regarded to play a crucial role [(129)]. NO is thought to be a fundamental mediator of cervical ripening.[(128)] As the ideal cervical-ripening agent is one that induces cervical remodeling without stimulating uterine activity, NO donors may be such agent as they relax the myometrium while inducing cervical ripening.

Although PGs are effective cervical-ripening agents, they are associated with several adverse effects, such as gastrointestinal symptoms, fever, pain, and high incidence of uterine tachysystole, hyper stimulation, and even uterine uterine rupture. [(130)]

Our study demonstrated that outpatient use of IMN has a significant effect in cervical repining and Bishop Score after 24 hours of administration in posterior cervix. In our study 30 women (60%) in the IMN group in contrast to 10 women (20%) in the placebo group had positive cervical repining after 24 hours (p=0.001*). These results are consistent with previous studies were done by Erling Ekerhovd et al, study in 2003.[(132)], Maria Bullarbo,[(133)] and Rameez study in 2007, which concluded that outpatient cervical ripening followed by labor induction with isosorbide mononitrate seems to be an effective, safe and well tolerated procedure. [(134)]Another study done by Eddama et al, demonstrated that the proportion of women with an unripe cervix after 24 h of outpatient treatment was significantly lower in the IMN group as compared with the placebo group (64% vs. 77%, *P* = 0.02).[(135)]

In our study there was a significant difference between the IMN group and the controls with respect to the Bishop score (4.40 vs. 3.68, *P* = 0.031*), which was consistent with Hamideh Yazdizadeh et al, study in which There was a significant difference between the IMN group and the control group with respect to the Bishop score (4.92 vs. 4.03, *P* = 0.0.01).[(136)] In another study done by Kavita Agarwal et al, the Bishop score was significantly improved 24 hours after initiation of the outpatient IMN treatment (*P*<0.001) and the needs for further cervical ripening and oxytocin infusion were less in the study than in the control group (*P*<0.001 and *P*=0.008). [(137)]

In Maria Bullarbo et al, study of post-term pregnancies, 22% of women treated with isosorbide mononitrate went into labor within 24 h, [(133)] a finding that was not demonstrated in our study. In contrast to the results of Bollapragada et al, study refute any significant difference between IMN and placebo groups regarding the admission to delivery interval. [(138)]

A randomized comparison study of IMN and PGE2 gel for cervical ripening was done by Kavita Agarwal et al, results in PGE2 group had significantly higher post ripening mean Bishop score, shorter time from start of medication to vaginal delivery and shorter labor-delivery interval compared to IMN group However, PGE2 group also had

significantly higher incidence of uterine tachysystole (15%) and non reassuring fetal heart (11%) compared to none in IMN group, as well as higher caesarean section rate (27% versus 17%).[139]

In 2011, the study was done by Mohamad S. Abdellah et al, demonstrated that women receiving IMN plus misoprosol showed significant changes in Bishope score 6 hours after administration as compared to misoprostol plus placebo significantly shorter intervals from the beginning of the induction to the beginning of the active phase of labor and from the beginning of the induction to delivery, no significant different in the incidence of tachsystols and hyperstimulation . Regarding headache, much more women suffer from headache in IMN group. [140]

In our study there were no significant differences between the two groups as regard to the mean age, parity and BMI, which was consistent with the previous study done by Mohamed Furukan *et al*, study. [134]

In our study 32 women treated with IMN went into normal labor compared to 26 women in the placebo group ($p>0.05$), there was no significant differences as regard to normal labor rate .However, Maria Bullarbo *et al*, study reported that 22 women treated with IMN went into labor compared to 8 women in the placebo group ($P < 0.05$). In women who did not go into labor cervical status was similar in the 2 groups the next day.[133]

In Mohamed Furukan et al, study there was marked increase in the proportion establishing spontaneous labor (28% *vs* 7.5%, $P < 0.01$) and cervix being favorable for oxytocin infusion (40% vs 9% $P < 0.001$) 2 days after therapy, in the same study the cesarean section rates were similar in both groups. [134]

In our study there was no significant differences in cesarean delivery rate, (36.0%vs 48%,$p>0.05$), neonatal outcomes and apgar score between the two groups, which was consistent with Sherif M. Habib et al, study there was no significant differences in cesarean delivery rate and neonatal outcomes. [141]

In the other hand, Sanchez-Ramos study demonstrated that misoprostol use had a significantly lower overall cesarean rate and a higher incidence of vaginal delivery within 24 hours of misoprostol application but use of misoprostol was associated with a higher incidence of uterine tachysystole. [142]

The most common side effect in women treated with isosorbide mononitrite was headache, experienced by 35women (70%) compared to 4 women (8%) in placebo group (($p< 0.05$) the intensity of headache was from mild to moderate headache. However in Maria Bullarbo et al, study reported more higher incidence (88%) of women treated with isosorbide mononitrite was complain from headache compared to (4%)in placebo group.[133]

Nicoll et al, studied the hemodynamic effect of vaginal isosorbide mononitrate and reported an increase in heart rate and reduction of blood pressure, but these effects were not clinically significant, [143] which was consistent with our study, there was no significant change in maternal blood pressure. These minor adverse effects were similar to a lot of previous report.

We confirmed our own work and the work of others demonstrating that IMN is an effective cervical ripening agent when measured by Bishop Score.

For post dates pregnancy, our own belief is that patient satisfaction, achieving vaginal (rather than cesarean) delivery and minimizing adverse events in mother and baby are all important outcomes. We suggest that there should be discussion and consensus among healthcare providers as to what the best outcome measures might be.

# SUMMARY

Postmaturity is the condition of a baby that has not yet been born after 42 weeks of gestation or 294 days past the first day of the mother's last menstrual period. Post term may be in itself high risk. The incidence of post-term pregnancy has been found to be as high as 3% to14% in some observational studies.

There were physiological changes occur with posttmatrity:

- Placental changes: aging, infarction and calcification.
- Amniotic fluid changes: oligohydraminies, cord compression and meconium aspiration syndrome, aspiration of thick meconium may cause severe pulmonary dysfunction and neonatal death.
- Fetal changes: malnutrition, macrosomia and shoulder dystopia may develop.

Post-term pregnancy is the most common indication for induction of labor. Compared with waiting indefinitely or waiting at least one week for labor to occur spontaneously, labor induction after 41 weeks of gestation is associated with fewer prenatal deaths and cesarean section rate. Labor induction can help reduce the need for additional monitoring of women and reduce the duration of hospitalization.

Inducing labor is artificially starting the labor process by using medication and other techniques. Although there is no ideal predictor of successful induction of labor, cervical status is now accepted as the most useful characteristic.

The uterine cervix has a pivotal role in the physiology of gestation and parturition; it has to be firm enough to retain the conceptus throughout pregnancy and, on the other hand, have the ability to soften before and during labor to enable the birth of the infant. Cervical ripening is actively controlled and shows features similar to those in inflammation in rearrangement of the cervical collagen fibers. Cervical ripening is thus associated with changes in local cytokines, prostaglandins, and metalloproteases, as well as in other bioregulators that play roles in inflammation and in collagen metabolism, these factors also take part in the regulation of Nitric oxide (NO) synthesis and release. Cervical NO plays a role in ripening of the human uterine cervix. The present study was designed to clarify this question. Assessment of cervical repining with Bishop Score can help to predict whether or not an induction is likely to succeed or fail. Cervical ripening is stimulated by:

- Non pharmacologic methods: herbal compounds, castor oil, hot baths, enemas, sexual intercourse and breast stimulation.
- Surgical methods: stripping of the membranes, amniotomy, and balloon catheter.
- Pharmacologic methods: Prostaglandins, Mifepristone, relaxin and oxyotcin.

Prostaglandins (PGs) E2 (Misoprostol) is the most commonly used drugs for preinduction cervical ripening usually administrated into the posterior fornix of vagina. Although PGs are effective cervical-ripening agents, they are associated with several adverse effects, such as gastrointestinal symptoms, fever, pain, and high incidence of tachysystole, uterine hyperstimulation, and even uterine rupture.

The ideal agent for cervical ripening would induce adequate cervical ripening with minimal adverse effects to the mother and the fetus. An increasing body of evidence

indicates a pivotal role of NO in the process of cervical ripening .Many investigators have proposed that Nitric oxide donors might be such agents.

The human uterine cervix is capable of producing NO, a free radical gas with an ultra-short half-life. NO acts as immunological mediator plays a crucial role in the cervical repining process. Cervical NO releases was induced by spontaneous uterine contractions and by cervical manipulation. Cervical NO release became stimulated during both physiological and pharmacologically induced cervical ripening in pregnant women.

Vaginal administration of nitric oxide reduces the cervical resistance without inducing uterine hyperstimulation,or abnormal fetal heart rate. Nitric oxide donors are class of drugs that exert their action by librating nitric oxide in vivo.They include sodium nitroprosside, nitroglycerin and isosorbide dinitrate and mononitrate.

The aim of this study is to assess the efficacy of the nitric oxide donor isosorbide mononitrate (IMN) on cervical ripening at 41 weeks 'gestation.

This study was conducted on 100 pregnant women recruited from the outpatient clinic all cases pregnant at 41 weeks gestational age, uncomplicated singleton pregnancy, cephalic presention, intact membrens and not in labor. Cases divided into 2 groups in first group 40 mg isosorbide mononitrate( IMN) tablet applied vaginally in posterior fornix, and in second group placebo applied vaginally in posterior fornix. Follow up the cervical status after 24 hours of administration, the patient were asked about new symptoms especially headache, palpitation, dizziness or abdominal pain and mode of delivery were assessed.

The present study demonstrated that outpatient use of IMN has a significant effect in cervical repining and Bishop Score after 24 hours of administration in posterior cervix. 30 women (60%) in the IMN group had positive cervical repining after 24. There were no significant differences in regarded to normal delivery rate, cesarean delivery rate, neonatal outcomes or apgar score.

The most common side effect in women treated with IMN was headache, experienced by 35women (70%), no significant change in maternal blood pressure or pulse rate.

We confirmed our own work and the work of others demonstrating that IMN is an effective cervical ripening agent, safe and appropriate for use as an outpatient procedure.