Original Research Article

Incidence of meconium stained liquor and foetal outcome in induction of labour with misoprostol vaginally

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Abstract

Background: Induction of labour is done to have safe timely delivery so that there is minimal risk to mother and the baby. Among various agents available for induction, Misoprostol is a safe and very effective agent with short induction delivery interval and successfully induce vaginal delivery within 24 hrs. Low dose of misoprostol is associated with minimal uterine stimulation with good fetal outcome despite increases incidence of meconium stained liquor. **Aim:** To evaluate the incidence of meconium stained liquor and fetal outcome in labour induced with Misoprostol vaginally. **Materials and Methods:** This is a prospective study included 150 pregnant women with 37 completed weeks who were induced with misoprostol. Study population was divide into two groups based on Bishop's score as unfavourable cervix and favourable cervix groups. Induction interval, mode of delivery, number of misoprostol doses, incidence of MSL, NICU admissions and APGAR scores were the different outcomes compared between the two groups. **Results:** Among the outcomes compare between unfavourable and favourable cervix groups induction delivery interval, number of misoprostol doses required for induction and incidence of MSL were more in the unfavourable cervix group and p values were statistically significant. Long induction delivery interval and higher number of misoprostol doses were associated with higher incidence of MSl. In terms of parity incidence of MSL was higher in primi with infavourable cervix while incidence of MSL was not significant between primi and multi in favourable cervix group. Among high risk population, incidence of MSL was higher in unfavourable group though distribution of risk population was similar in both groups. there was no significant difference in other foetal outcomes between the two groups. **Conclusion:** Misoprostol is an effective priming and labour inducing agent which fulfils all the criteria of an inducing agent. Though incidence of MSL is higher in misoprostol induced labour among women with unfavourable cervix, the fetal outcomes seems to be very good.

Key Words: Misoprostol

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Received Date: 08/09/2018 Revised Date: 14/10/2018 Accepted Date: 01/11/2018
DOI: https://doi.org/10.26611/1012821

Access this article online

Quick Response Code:

Website: www.medpulse.in

Accessed Date: 05 November 2018

INTRODUCTION

Ideally a pregnancy should reach till completion of full term or at least till 37 weeks for the baby to survive once it comes out of mother womb. Situations often arise in obstetrics where it become necessary to interrupt a pregnancy in the interest of the mother and/ or the baby. Ultimate goal is to have safe timely delivery so that there is minimal risk to mother and the baby. This is where induction of labour comes in co picture. Induction of labour constitutes initiating effective uterine contraction which will help in cervical dilation and eventually ending in delivery of baby per vaginally before the onset of spontaneous labour. A number of clinical conditions often

How to cite this article: B ArunaKumari, Nagamani. Incidence of meconium stained liquor and foetal outcome in induction of labour with misoprostol vaginally. *MedPulse – International Journal of Gynaecology.* November 2018; 8(2): 32-39.
http://medpulse.in/Gynacology/index.php

pose potential risks to the mother and the baby if pregnancy is continued, and so induction of labour is in indicated or opted for. In some situations induction of labour is done for patient's or obstetrician's convenience.[1] However, induction of labour is not completely free of risk. One has to keep in mind the potential risks such as failure if induction is ending in caesarean section, possibilities of preterm delivery and risks of hyperstimulation leading to fetal hypoxia and even death. Hence there is need for safer and effective means of inducing labour. Various methods have been in use for ages, out of which Oxytocin + Prostaglandins + ARM have been in use. Prostaglandins have the advantage of ripening the cervix before the onset of labour pains. This study was aimed at finding out the induction delivery interval and incidence of meconium stained liquor and its significance on the neonatal outcome in misoprostol induced labours.

AIMS AND OBJECTIVE

To evaluate the incidence of meconium stained liquor and fetal outcome in labour induced with Misoprostol vaginally.

MATERIALS AND METHODS

Prospective randomized controlled study consists of 150 women who were randomly selected and with gestation age of more than 37 completed weeks. This study was conducted from January 2013 to September 2014.These women were divided in to 2 groups, with 75 women in each group. 1st Group consists of women with unfavourable cervix (bishop score </=4). High risk groups of Pre-eclampsia/Gestational Hypertension, past-EDD, oligohydramnios, IUGR, post-term, and PROM were included in this group for induction of labour. 2nd Group consists of women with favourable cervix (bishop score >4). High risk groups of Pre-eclampsia/Gestational Hypertension, past-EDD, oligohydramnios, IUGR, post-term and PROM was included in this group for induction of labour. Selected women were with 37 completed weeks and singleton pregnancy and vertex presentation and no contraindication for vaginal delivery. Gestational age of more than 37weeks**,** Single viable fetus with vertex presentation, No malpresentation, No contraindication for vaginal delivery like CPD / contracted pelvis, Absence of abnormal vaginal bleeding, abruption placenta, placenta previa,chorioamnionitis, No evidence of symptoms of fetal distress, No contraindication for use of prostaglandins like asthma, glaucoma, No fetal malformations. Women who were taken as a part of study were subjected to basic pelvic examination to rule out contracted pelvis and other abnormalities of pelvis and its organs. Each patient was assigned a Bishop's score based on the cervical status. Women with advanced Bishop's score were also included in the study, provided they had no contraindications. Each women had received 25ug of misoprostol (every 4rd hourly) placed digitally in the posterior fornix of the vagina for the maximum of 6 doses. Every ½ hourly fetal heart rate is monitored along with nature of uterine contractions to detect any uterine tachysystole/ hyperstimulation or fetal heart rate variability. Every 4th hourly another pelvic examination is done to note the progress of labour in terms of dilation, effacement and descent of the presenting part and 25ug of misoprostol is repeated. At about 3-4cm of cervical dilatation, if the membranes have not been ruptured spontaneously an artificial rupture of membranes was done to note the colour of liquor and its correlation with fetal heart rate. Then depending on the colour, fetal heart pattern. (tachycardia, Bradycardia/ fetal rate variability). Patient was taken for caesarean section or allowed to continue for vaginal delivery. If there is fetal distress, tachysystole or hyper stimulation, next dose of misoprostol should not be repeated. After the baby delivered, birth Apgar of 1 minute, 5 minutes and 10 minutes was recorded. Babies with MSL and any other complication were shifted to NICU for observation. Induction was considered to have succeeded when there is improved Bishop's score resulting in successful vaginal delivery occurred within 24 hours.

Following parameters were evaluated

1. Time interval from the onset of induction to delivery.
2. Number of Misoprostol doses.
3. Mode of delivery vaginal / instrumental delivery or caesarean section and indication for the same
4. Uterine contraction abnormalities.

A. Tachysystole — 6 or mote contraction in a 10 minutes interval for 2 such consecutive intervals.

B. Hypersystole — A single contraction lasting more than 2 minutes.

C. Hyperstimulation — any of the above with fetal heart rate abnormalities.

5. Any prostaglandin related side effects such as hyperpyrexia, vomiting and diarrhoea.
6. Incidence of fetal distress Bradycardia / tachycardia.
7. Incidence of meconium liquor and fetal outcome.
8. Neonatal outcome in respect to Apgar score as associated with admission to NICU.

RESULTS

During the period of study from January 2013 to September 2014, a total number of 150 women were studied. 150 women received 25ug of Misoprostol and the number of doses of Misoprostol were decided depending

upon the progress of labour and cervical status. These women were compared with respect to age, parity, cervical status, mode of delivery, induction to delivery time, the total number of doses required, incidence of meconium, maternal and fetal complication.

Table 1: Age and parity distribution of the study groups

Age	Group1	Group2	P-Value
<20yrs	2 (2.7%)	4 (5.3%)	4 (5.3%)
20-30yrs	72 (96%)	71 (94.6%)	71 (94.6%)
>30yrs	1 (1.3%)	0 (0%)	0 (0%)
Parity			
Primi	47 (62.3%)	44 (58.7%)	44 (58.7%)
2nd Gravida	20 (26%)	23 (30.6%)	23 (30.6%)
3rd Gravida	8 (10.7%)	8 (10.7%)	8 (10.7%)

Majority of cases in group 1and group 2 are in the age group of 20-30yrs. In the 2 groups prim gravida constitute the major part with 47 cases in Group-I, 44 cases in Group-II. Statistical analysis has been done for the 2 Groups. This suggests similar distribution of cases based on parity.

Table 2: Indication for usage of misoprostol in study groups

Indication	Number of Cases In Group1	Number Of Cases In Group2
PE/GHTN	26 (34.7%)	24 (32%)
Past-EDD	19 (25.3%)	20 (26.7%)
Oligohydramnios	8 (10.7%)	6 (8%)
IUGR	6 (8%)	7 (9.3%)
Post-term	4 (5.3%)	4 (5.3%)
PROM	12 (16%)	14 (18.6%)

There is no significant difference of high risk population present in above two groups. The most common cause for indication was pregnancy induced hypertension followed by past EDD in both groups 1 and 2.

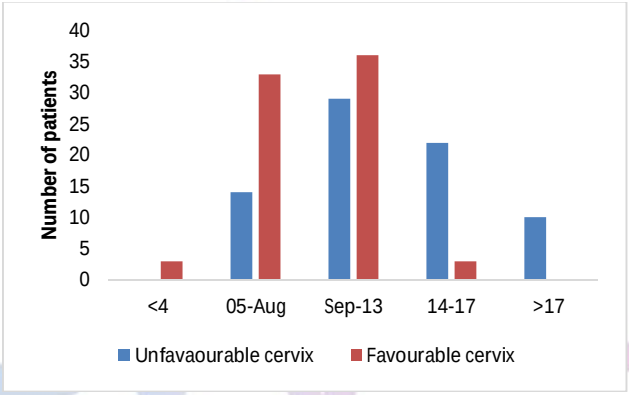

Figure 1: Induction to Delivery Time in both groups.
T-test value is 6.478 p value is <0.05 significant

The average time from induction to vaginal delivery was 12.87+/-4.65 hours in group1 (unfavourable cervix) and 8.85+/-2.68 hours in group2 (favourable cervix), induction delivery interval is longer in unfavourable cervix group than favourable cervix group. The average time from induction in group -1 to vaginal delivery was 13.95+/-4.48 hours in multigravida and 11.05+/-4.40 hours in multigravida. Induction delivery interval is longer in nulliparous women than multigravida. The average time from induction in group -2 to vaginal delivery was 9.68+/-2.77 hours in nulligravida and 7.67+/-2.056 hours in multigravida. Induction delivery interval is longer in nulliparous women than multigravida.

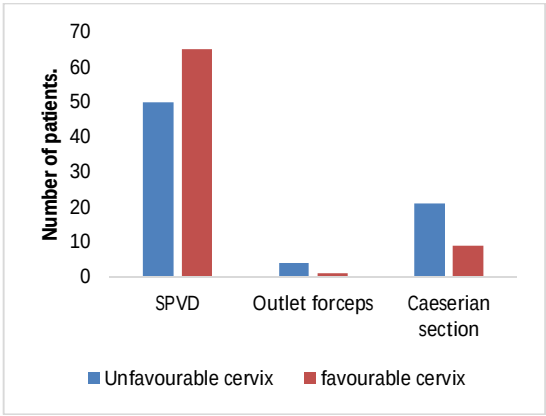

Figure 2: Mode of delivery in both groups
T-test value is 2.79 p value is <0.05 Significant

In unfavourable cervix group caesarean section rate is higher than favourable group. The most common indication for caesarean section was failure to progress followed by MSL and fetal distress. Neonates who had fetal distress and underwent caesarean section were born

with good Apgar. In favourable cervix parity of women influence the mode of delivery as shown by p value above the most common indication for caesarean section was thick MSL with fetal distress.

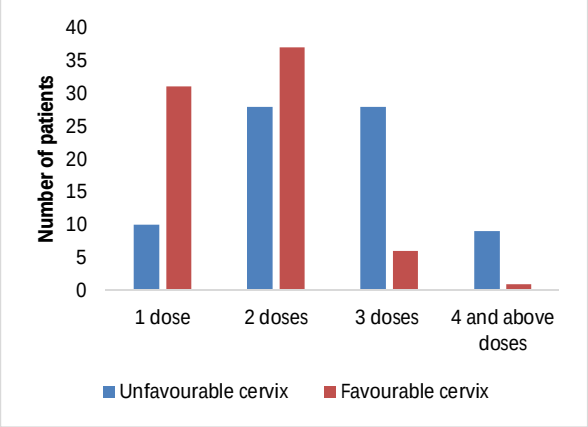

Figure 3: Number of doses of Misoprostol
T-test value is 6.099, p value <0.05, Significant

The average number of Misoprostol doses required for vaginal delivery in group 1 is 2.50+/-0.93 in group 2 it is 1.69+/-0.67. The average number of doses required for vaginal delivery in group-1 case of nulligravida is 2.72+/-0.926 whereas in case of multigravida, it is 2.14+/-0.84doses. The average number of doses required for vaginal delivery in group-2 of nulligravida is 1.90+/-0.67 whereas in case of multigravida, it is 1.38+/-0.55 doses.

Table 3: Maternal Complications in study groups

Complication	Group 1 n (percentage)	Group 2 n (percentage)
Hyperstimulation	4 (5.3%)	2 (2.6%)
Tachysystole	2 (2.6%)	1 (1.3%)
Diarrhoea	3 (4%)	2 (2.6%)
Vomiting's	5 (6.6%)	2 (2.6%)
Hyperpyrexia	2 (2.6%)	0

Table 4: Incidence of Meconium Stained Liquor based on indication of induction

High Risk Cases	Number of Cases	Incidence of MSL
Group 1		
PE/GHTN	26	11 (42.3%)
Past EDD	19	6 (31.6%)
Oligo	8	1 (12.5%)
IUGR	6	1 (16.7%)
Post-term	4	3 (75%)
PROM	12	1 (8.3%)
Group 2		
PE/GHTN	24	6 (25%)
Past EDD	20	2 (10%)
Oligo	6	1 (16.7%)
IUGR	7	0
Post-term	4	2 (50%)
PROM	14	1 (7.1%)

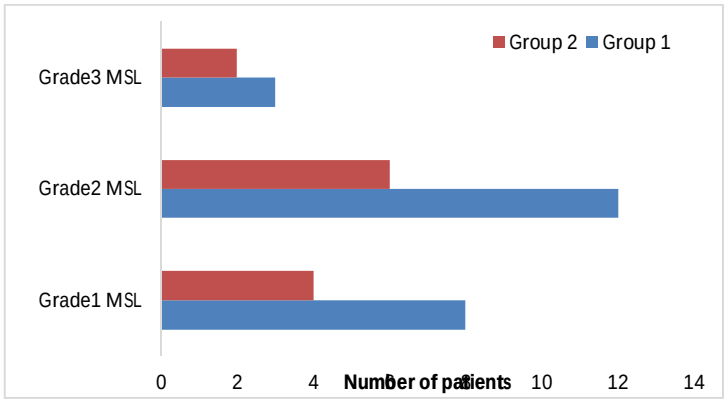

Figure 4: Incidence of Meconium Stained Liquor among the groups
Chi square test value is 4.509, 'p' value is <0.05, significant

The total incidence of meconium stained liquor was about 30.7% in case of Group-I and 16% in Group II. In unfavourable group, incidence of MSL is more in Nulligravida (41.9%) than Multigravida (15.8%).

Table 5: Neonatal Outcome According To Grades of Meconium Stained Liquor

Grade of MSL	NICU admissions	APGAR <7 at 5mins	Meconium aspiration syndrome	Neonate after 1 week
Group-1				
Grade 1 MSL	8	0	0	Baby well with mother
Grade 2 MSL	12	3	3	1 Babies in NICU and others well with mother
Grade 3 MSL	3	2	2	1 Babies in NICU and others well with mother
Group-2				
Grade 1 MSL	4	0	0	Baby well with mother
Grade 2 MSL	6	2	1	Baby well with mother
Grade 3 MSL	2	1	1	Baby well with mother

In group 1five cases had meconium aspiration syndrome and APGAR <7 at 5mins. All of them (meconium stained liquor babies) were admitted to NICU and after 1 week 2 babies was still admitted in NICU while the other babies were discharged and were healthy with their mothers, There were no perinatal deaths. In group2 two cases had meconium aspiration syndrome. All of them (meconium stained liquor babies) were admitted to NICU and after 1 week only 1 baby was admitted in NICU while other babies were discharged and were healthy with their mothers. There were no perinatal deaths. In addition, 3 babies were admitted to NICU in view of low birth weight and IUGR.

DISCUSSION

Prostaglandins score over other methods of induction in the presence of unripe cervix. They have a dual advantage of ripening the cervix as well as inducing myometrial contractility. Ideal inducing agent is that will have shorter induction delivery interval, absence of side effects with good maternal and fetal outcome and convenience to both doctor and patient. Among the emerging Prostaglandins misoprostol was found to be efficacious than other. Previous reviews have shown a trend towards more meconium passage with Misoprostol than with other agents. Various dose regimens have been used for misoprostol in different studies. In the past, dose of 100µg was often used in clinical studies. As more data became available regarding adverse effects and safety profile the dose of 100µg is replaced by 50 and 25µg in clinical studies. Several meta-analysis were done comparing 25 and 50µg doses. McMaster K, Sanchez-Ramos L, Kaunitz[2] performed a meta-analysis of 13 studies including 1945 women comparing 25 versus 50 micrograms of intravaginal misoprostol tablets for the induction of labour. The study concluded an improved safety profile with 25 micrograms, with decreased rates of tachysystole, hyper stimulation, caesarean deliveries for non-reassuring FHR, NICU admissions and meconium passage (RR 0.65; 95% CI 0.45-0.96). In the current study, a dose of 25µg of misoprostol has been used intravaginally every 4hrs for the maximum dose of 6 doses. (Over 24hr period).This dose of misoprostol (25µg 4hrly, max-6doses) was found to be safe, efficacious and has low incidence of side effects with good maternal and fetal outcome. Our study is comparable to Gregson *et al* 2005 [3]and Eroglu *et al* [4]2007 who had used 25 µg of tablet 4rd hourly max 6 doses. A recent ACOG committee opinion states that if misoprostol is used for cervical ripening and labour induction, 25 µg should be considered for initial dose. This opinion is based on greater incidence of Tachysystole and Hyperstimulation noted with larger doses of misoprostol.

Table 6: Oral versus vaginal administration of misoprostol in various studies

Study	No of Patients	Oral dose	Vaginal dose	Result
Toppozada *et al*[5]	40	100µg3hrly	100µg3hrly	Vaginal is more effective
Adair *et al* [6]	178	200µg	50µg, 6hrly	Similar efficacy, Oral has more tachysystole, hyperstimulation.
Wing *et al*[7]	220	50µg,4hrly	25µg,4hrly	Oral dose less effective than vaginal
Bennett *et al*[8]	206	50µg,4hrly	25µg,4hrly	Shorter interval with vaginal dose
Dyar *et al*[9]	153	50-100µg,4th hrly	25µg,4hrly	Equally effective (more tachysyole with oral dose)

So the oral dose is associated with more side effects and have longer interval for vaginal delivery than vaginal dose. In the current study, out of 150 cases, 119 cases (79.3%) cases delivered by spontaneous vaginal delivery without significant increase in hyperstimulation and tachysystole. Several authors like Sanchez Ramos *et al*[2], Kadanali *et al*[10] have reported better Scores 4-6 hours after start up induction. While Fletcher *et al*[11] reported significantly better Score after 12 hour induction, wing *et al* reported better scores prior to Oxytocin Augmentation. In the current study out of 150 cases, only 12 cases (8%) had poor Bishop's score after 8 hours of induction.

Table 7: Induction delivery interval of different trails

Authors	Induction Delivery Interval
Elhassan *et al* 2005[12]	21.9±4.2 hrs
Krupa *et al* 2005[13]	18.9 hrs
Ortiz *et al* 2002[14]	7.9 hrs
Kidanto *et al* 2006[15]	10.86 hrs
Clark *et al* 1998[16]	19.68 hrs±9.4 hrs
Wing *et al* 1998[7]	13.5±8.5 hrs
Kumar *et al* 2001[17]	21.9 hrs ±8mins
Current study	
Group 1	12.87hrs
Group 2	8.85hrs

Variations in the bishop score before induction, dosing interval, and giving of oxytocin augmentation might have all contributed to this difference in the induction delivery interval. The current study is comparable with that of Wing *et al*[7], Kidanto et at [15]and Ortiz *et al*[14] With the induction delivery interval falling in between 8-13hours. Induction delivery interval was shortest in favourable cervix group followed by unfavourable group. The difference in the induction delivery interval between the groups shows statistical significance of values. Among 23 Meconium stained liquor cases in

unfavourable cervix group, 65% of them had induction delivery interval of more than 14hrs (mean induction delivery interval is 12.87hrs).Among 12 Meconium stained liquor cases in favourable cervix group, 66% of them had induction delivery interval of more than 9hrs. (Mean induction delivery interval is 8.85hrs). This signifies that incidence of Meconium stained liquor is greater in women with longer induction delivery interval.

Table 8: Caesarian Section in unfavourable cervix

Authors	Caesarian Section in unfavourable cervix
Elhassan *et al* 2005[12]	32.3%
Wing *et al* 1996[7]	21.2%
Current study	
Group 1	28%
Authors	
(studies with bishop score <7)	
Eroglu *et al* 2007[4]	19.1%
Clark *et al* 1998[16]	15%
Wing *et al* 1998[7]	21.2%
Has 2002[18]	20.6%
Current study	
Group 2	12%

Caesarean section rate in the current study was comparable to that of Elhassan *et al*[12] and Wing *et al*.[18] Caesarean section rate in the current study was comparable to that of Eroglu *et al*[4] and Clark *et al*[16]. Among other studies caesarean section rate was higher due to high proportions of primigravida cases and women with bishop score <4. Caesarean section rate was comparatively more in primigravida. This can be explained by the unfavourable cervix as well as undiagnosed cephalo pelvic disproportion. In the current study caesarean section rate was higher in unfavourable group than favourable group which was statistically significant.

Table 9: Incidence of uterine hyperstimulation and tachysystole

Authors	Dose regime	Hyperstimulation	Tachysystole
Wing *et al* 1996[7]	25µg 3hrly max-8 doses	2.7%	11.1%
Eroglu *et al* 2007[4]	25µg 4hrly max-6 doses	0	2.7%
El-Sherbiny *et al* 2001[19]	25µg 4hrly max-6 doses	0	10.7%
BUSER *et al*[20]	50µg 4hrly	18.4%	7.8%
Current study			
Group 1	25micgms 4th hrly 6doses	5.3%	2.6%
Group2	25micgms 4th hrly 6doses	2.6%	1.3%

In the current study, incidence of hyperstimulation was similar to other studies who used the same dose of Misoprostol. With exception of Buser *et al*[20] study, there is low incidence of hyperstimulation and tachysystole in all other studies. Incidence of hyperstimulation and tachsystole was higher in Buser *et al*[20] studies because of high dose of misoprostol used. In the current study Incidence of hyperstimulation was more (8%) in unfavourable group than in favourable group (2.6%) This might be explained by high average number of doses in unfavourable group. Overall incidence of hyperstimulation in misoprostol induction group (group 1, 2) is 5.3% whereas the overall incidence of MSL (in group1 and 2) is 23.3%. This discrepancy suggests that uterine hyperstimulation may not be the cause of MSL in the current study. Although it has been demonstrated that the passage of meconium is very late phenomenon after hypoxia as occurred, it is far more common to note the presence of meconium in the absence of hypoxia. While hypoxia may play a part in the release of meconium into amniotic fluid, its role in causing the aspiration of meconium is more established fetuses inhale amniotic fluid and meconium by either gasping or deep breathing movements Babies who aspirate meconium but are not hypoxemic during labour are unlikely to suffer any serious consequences and 90% will be asymptomatic. In the current study, incidence of Meconium stained liquor in women with unfavourable cervix was similar to Wing *et al*.[7] Compared to other studies, incidence of Meconium stained liquor was higher in the current study because of discrepancy in the selection of high-risk group. Though the percentage of incidence of Meconium stained liquor was higher, it was not statistically significant. In group 1, grade 1 MSL was found in 8cases, grade 2 MSL was found in 12 cases and grade 3 MSL was found in 3cases. Out of these, 5 cases had meconium aspiration syndrome and APGAR <7 at 5mins. All of them were admitted to NICU and after 1 week 4 babies was still admitted in NICU while the other babies were discharged and were healthy with their mothers. In group 2, grade 1 MSL was

found in 4cases, grade 2 MSL was found in 6 cases and grade 3 MSL was found in 2 cases. Out of these, 2 cases had meconium aspiration syndrome and APGAR <7 at 5mins. All of them were admitted to NICU and after 1 week only 1 baby remained in NICU while other babies were discharged and were healthy with their mothers. Among 2 groups, there is high incidence of MSL in Unfavourable cervix group than favourable cervix group. Group 1 has increased incidence of MSL than group2 (30% vs. 18%). This is explained by higher induction delivery interval and higher average number of misoprostol doses required in unfavourable group. In unfavourable cervix group, 15 cases had induction delivery interval of more than 14hrs and needed more misoprostol doses.

Table 10: Apgar<7 at 5 min and NICU admission in misoprostol induced labour in various studies

Authors	APGAR <7 at 5mins
Filho 2007[21]	3.3%
Has 2002[18]	5.1%
El-Sherbiny 2001[19]	2.1%
Wing 1996[7]	1.5%
Current Study	
Group 1	6.6%
Group 2	4%
NICU admissions	
Eroglu 2007[4]	0
Has 2002[18]	5.1%
El-Sherbiny 2001[19]	11.8%
Wing 1996[7]	20.8%
Current Study	
Group 1	30.6%
Group 2	16%

In the current study, incidence of APGAR <7 at 5 mins was 6.6% and 4%. The incidence in group 1 is higher compared to the other studies because the study population had variable distribution of high-risk groups. Incidence of Meconium stained liquor was higher in the current study compared to other studies. NICU admissions were higher in the current study compared to other studies mentioned in the table. Though majority of these infants had good Apgar scores, all of them were admitted to NICU for observation. The reason for this was the policy of routine admission to NICU, of infants with meconium stained liquor in our hospital.

CONCLUSION

In current study of 150 cases, comparison of women with unfavourable cervix and favourable cervix group showed no significant difference in maternal age and parity. Similarly, majority of women in both groups delivered via caesarean section (56%) with indication being mainly on fetal grounds and worsening maternal condition. Incidence of Meconium stained liquor is also influenced by the indication of induction. Pre-ecampsia and post-term cases have higher incidence of Meconium stained liquor. The distribution of high-risk population in group1 and group2 had been similar with no statistical significance so as to eliminate the bias in comparison of the two groups. The current study evaluates the effect of bishop score on incidence of Meconium stained liquor and neonatal comes. Misoprostol is an effective priming and labour inducing agent which fulfils all the criteria of an ideal inducing agent. The higher incidence of meconium associated with misoprostol is due to the action of the drug on the gastrointestinal tract of the fetus. Hence the neonatal outcome is good with Misoprostol.

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Source of Support: None Declared
Conflict of Interest: None Declared