

# Effect of Misoprostol in Third Trimester of Pregnancy- A Multi-Center Study in Bangladesh

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## Abstract

**Background:** Misoprostol is an analogue of prostaglandin (PGE<sub>1</sub>) and the first registered PGN used for the treatment of peptic ulcer disease. Misoprostol should not be used in pregnant women but it can be used in termination of intrauterine fetal death (IUFD). It has been used for the induction of abortion in the first and second trimester of pregnancy. Misoprostol has already been proved to be effective and efficient for second trimester since 1987. There is insufficient information available from clinical trials to support their use to induce labor in third trimester of pregnancy. **Aim of the study:** The aim of this study was to describe the effect of misoprostol in third trimester of pregnancy. **Methods:** This retrospective study was carried out in two large hospitals in Dhaka city, which is the capital of a South Asian country, Bangladesh. The record of the studied subject was taken from the Department of Obstetrics and Gynecology of Alpha Hospital and the maternity ward of Beta Hospital from June 2018 to August 2019. The actual names of the two hospitals are pseudonym for privacy. A detailed history of each patient was taken and physical and obstetric examination were done. In total 52 patients were investigated and data were analyzed by SPSS version 23.0. **Results:** In this study, the primi gravida response time was found as the highest. On an average 20.34 hours was needed for the primi gravida category. In single, 2 and multi-parity cases the average pain response times were found as 16.3125, 10.3375 and 14 hours respectively. In Primi, 2nd, 3rd and 5th gravida cases the average delivery times were found 13.0714, 12.5938, 9.0769 and 3 hours respectively. Against single, two and three doses of misoprostol, the average pain response times were found 7.6875, 11.5375 and 19.25 hours respectively. **Conclusion:** In this study, it had been found that, most of the patient of IUFD was 'primigravid' (30.8%) of total respondents having complication with medical and endocrinal disease. Pre- eclampsia is more common in prim gravid than multi. There is history of thyroid dysfunction. In some cases, now a day, GDM is the cause behind IUFD.

**Keywords:** Misoprostol, Pregnancy, Third trimester, Induction, Pain, Obstetrics.

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## INTRODUCTION

Misoprostol is an analogue of prostaglandin (PGE<sub>1</sub>) and the first registered PGN used for the treatment of peptic ulcer disease. Within the past two decades, prostaglandins (PGs) have provided as an alternative procedure for induction of labour in women with IUFD [1]. Misoprostol has been widely used for cervical ripening as well as labour induction in various pregnancy status at different gestational ages and using through different routes and dosing regimens [2].

Although misoprostol (15-deoxy-16-hydroxy-16-methylPGE<sub>1</sub>) is effective, concern has been raised regarding the widespread application of this agent as a primary or adjuvant agent for labour induction. [3] In spite of those concerns, a large number of evidence exists which shows that, the use of misoprostol as labour induction is highly safe and effective [4]. Misoprostol is usually absorbed rapidly when administered vaginally, orally or intra-cervically [5]. Among several routes, the vaginal route is comparatively advantageous because sustained for long,

peak levels are reached slowly and associated with fewer side effects [6]. In some other studies [7-11] it was reported that, the vaginal route is more effective than oral route. Zieman *et al.*, [12] compared the absorption kinetics of misoprostol with vaginal versus oral administration in pregnant women. In another study, it was found that, the systemic bioavailability of vaginally administered misoprostol is three-times higher than that of the oral route administration when determined by area-under-the-curve [13]. Although misoprostol combined with mifepristone may ensure better outcomes [14, 15], misoprostol alone is still the standard protocol worldwide, especially in the developing countries.

## OBJECTIVE

The objective of the study to evaluation the effect of misoprostol in third trimester of pregnancy among Bangladeshi women.

## METHODOLOGY

This retrospective study was carried out in two large hospitals in Dhaka city the capital of a South Asian country, Bangladesh. The record of the studied population was taken from the Department of Obstetrics and Gynecology of Alpha Hospital and the maternity ward of Beta Hospital from June 2018 to August 2019. The actual names of the two hospitals are pseudonym for privacy. The criteria for IUFD were after 28 weeks of gestation. Gestational age was based on reliable menstrual history and/or confirmation by ultrasonographic measurements performed in early pregnancy. Patient with history of previous two caesarian section, myometrial invasion of placenta, placenta previa and any critical emergency with obstetrical indication of immediate delivery was excluded from the study. A detailed history of each patient was taken and physical and obstetric examination were done. Baseline investigation was done according to hospitals protocol. Each of the studied women was given 200µgm of misoprostol

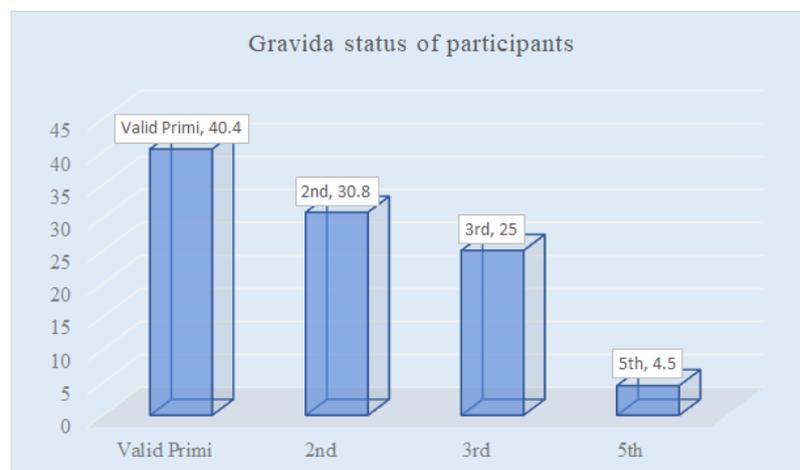
orally every 6 hours. At the time of inclusion, data on maternal and gestational age, parity, mode of previous delivery, complications of pregnancy and status of cervix were collected. In addition, after applying the medicine, the response for pain and time of delivery were recorded. A sample size of 6 years' patients was investigated and data was collected. Among those 56.3% were between 20 to 30 years of age and 43.7% was below 31 to 40 years old. The collected herd copy data record was then transcribed in MS-Excel.

## RESULT

In this study, among total 52 participants, 40% were valid primi cases. Besides this, 30.8%, 25% and 3.8% cases were with 2<sup>nd</sup>, 3<sup>rd</sup> and, 5<sup>th</sup> gravida respectively. In this study, the primi gravida response time was found as the highest. On an average 20.34 hours was needed for the primi gravida category. For the 2nd, 3rd and, 5th gravida average times were found 6.62±3.44, 4.69±0.95, 3±0 and 11.54±12.84 hours respectively. ANOVA test was conducted to verify whether the differences observed between the pain response time needed for the different gravida were truly significant or not. The result showed that, F value was 7.849 with sig 0.000, which indicates that the differences observed were the true differences in the population. In single, 2 and multi-parity cases the average pain response times were found as 16.3125, 10.3375 and 14 hours respectively. In Primi, 2nd, 3rd and 5th gravida cases the average delivery times were found 13.0714, 12.5938, 9.0769 and 3 hours respectively. Against single, two and three doses of misoprostol, the average pain response times were found 7.6875, 11.5375 and 19.25 hours respectively.

**Table 1: Gravida status of participants (N=52)**

Gravida	n	%
Valid Primi	21	40.4
2nd	16	30.8
3rd	13	25.0
5th	2	3.8



**Figure I: Gravida status of the Participants**

**Table 2: Average pain response time (hour) with respect to gravida (N=52)**

Gravida	n	Mean ±SD
Primi	21	20.33±16.51
2nd	16	6.62±3.44
3rd	13	4.69±0.95
5th	2	3±0
Total	52	11.54±12.84

**Table 3: ANOVA test on average pain response time (hour) with respect to gravida, (N=52)**

Variables	Sum of Squares	df	Mean Square	F	Sig
Between groups	2765.737	3	921.912	7.849	0
Within groups	5637.686	48	117.452		
Total	8403.423	51			

**Table 4: Doses required for effective termination, (N=52)**

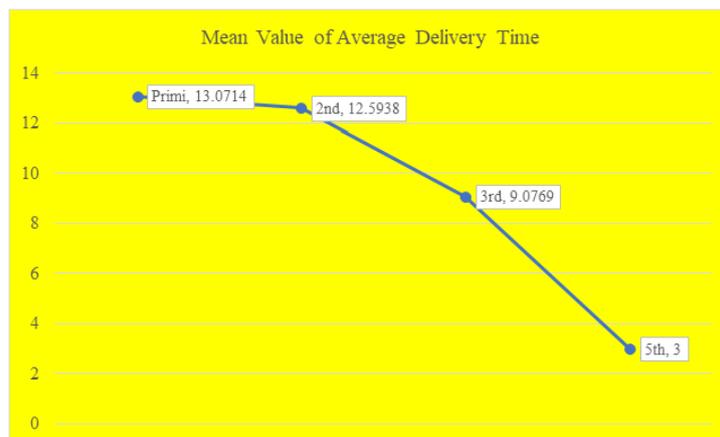
Gravida	n	Cumulative (%)
Valid Primi	21	40.4
2nd	16	71.2
3rd	13	96.2
5th	2	100

**Table 5: Average pain response time with respect to different parity and gravidas age of misoprostol doses, (N=52)**

Parity	n	Mean
1	8	16.3125
2	40	10.3375
Multi	4	14
Total	52	11.5385

**Table 6: Average delivery time with respect to gravida, (N=52)**

Gravida	n	Mean	(±SD)
Primi	21	13.0714	9.29689
2nd	16	12.5938	4.97064
3rd	13	9.0769	3.23938
5th	2	3.0000	0.0000
Total	52	11.5385	7.02506



**Figure II: Mean Value of Average Delivery Time of the Participants (N=52)**

**Table 7: Average pain response time with respect to different miso-doses (N=52)**

Dose	n	Mean	(±SD)
1	8	7.6875	3.44277
2	40	11.5375	6.7912
3	4	19.25	9.63933

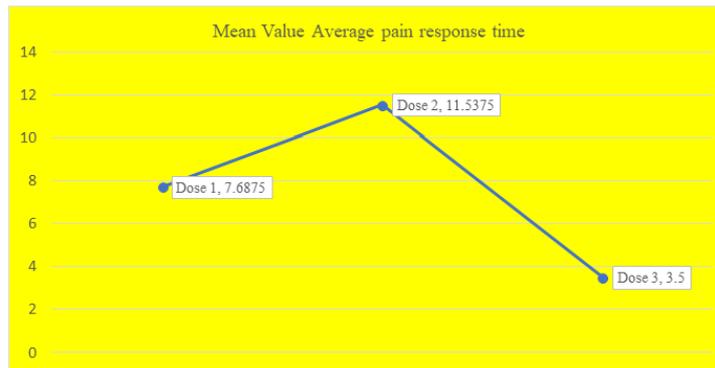


Figure III: Mean Value of Average Pain Responses of the Participants, (N=52)

## DISCUSSION

The aim of this study was to describe the effect of misoprostol in third trimester of pregnancy. In this study, among total 52 participants, 40% were valid primi cases. Besides this, 30.8%, 25% and 3.8% cases were with 2nd, 3rd and, 5th gravida respectively. The primi gravida response time was found as the highest (40%) and that was almost similar to the study by Jahanfar SH *et al.*, [16] in which the incidence of IUFD in primipara was 39.2%. In this current study, the most common cause of IUFD was idiopathic and that was the second most common cause of IUFD in Abdul *et al.*, study [17]. Among our settings, on an average 20.34 hours was in needed for the primi gravida category. For the 2nd, 3rd and, 5th gravida average times were found  $6.62 \pm 3.44$ ,  $4.69 \pm 0.95$ ,  $3 \pm 0$  and  $11.54 \pm 12.84$  hours respectively. But in Gomez *et al.*, study [18], 15% cases required >24 hrs. To deliver and/or extra augmentation. As the most common side effect, fever was seen in our study followed by diarrhoea which was similar to El Garib *et al.*, study [19]. In single, 2 and multi-parity cases of this study, the average pain response times were found as 16.3125, 10.3375 and 14 hours respectively. In Primi, 2nd, 3rd and 5th gravida cases the average delivery times were found 13.0714, 12.5938, 9.0769 and 3 hours respectively. Against single, two and three doses of misoprostol, the average pain response times were found 7.6875, 11.5375 and 19.25 hours respectively and these findings are comparable to that reported from Ibadan (Nigeria) of 17.5 hours [14] and Kampala of 14.7 hours [20]. Our mean onset of painful uterine contractions was also similar to that of Fawole and colleague's findings [21]. The effectiveness of misoprostol in management of fetal death and induction of labor in many other studies [15, 21, 22]

## LIMITATION OF THE STUDY

Though it was a single centered study with a small sample size, so findings of this study may not reflect the exact scenario of the whole country.

## CONCLUSION & RECOMMENDATION

In this study, it had been found that, most of the patient of IUFD was 'primigravid' (30.8%) of total

respondents having complication with medical and endocrinal disease. Pre- eclampsia is more common in prim gravid than multi. There is history of thyroid dysfunction. In some cases, now a day, GDM is the cause behind IUFD. We would like to recommend for conducting similar more studies with larger sized samples in several places, for getting more specific findings.

## REFERENCES

1. Kochenour, N. K. (1987). Management of fetal demise. *Clinical Obstetrics and Gynecology*, 30(2), 322-330.
2. Chittacharoen, A., Herabutya, Y., & Punyavachira, P. (2003). A randomized trial of oral and vaginal misoprostol to manage delivery in cases of fetal death. *Obstetrics & Gynecology*, 101(1), 70-73.
3. Arias, F. (2000). Pharmacology of oxytocin and prostaglandins. *Clin Obstet Gynecol*, 43(3), 453.
4. Hale, R. W., & Zinberg, S. (2001). Use of Misoprostol in Pregnancy. *New England Journal of Medicine*, 344, 59-60.
5. El-Gharib, M. N., El-Ebyary, M. T., Alhawary, T. S., & Elshourbagy, S. H. (2010). Low dose vaginal misoprostol in the management of women with intrauterine fetal death. *Clinical Medicine insights: Women's Health*, 3, CMWH-S5797.
6. Gottschall, D. S., Borgida, A. F., Mihalek, J. J., Sauer, F., & Rodis, J. F. (1997). A randomized clinical trial comparing misoprostol with prostaglandin E2 gel for preinduction cervical ripening. *American journal of obstetrics and gynecology*, 177(5), 1067-1070.
7. Jing, S. (2000). Use of misoprostol in Obstetrics and Gynaecology. *Obstet Gynecol Surv*, 55(8), 503.
8. Ho, P. C., Ngai, S. W., Liu, K. L., Wong, G. C. Y., & Lee, S. W. H. (1997). Vaginal misoprostol compared with oral misoprostol in termination of second-trimester pregnancy. *Obstetrics & gynecology*, 90(5), 735-738.
9. Ngai, S. W., Chan, Y. M., Lam, S. W., & Lao, T. T. (2000). Labour characteristics and uterine activity: misoprostol compared with oxytocin in women at term with prelabour rupture of the

- membranes. *BJOG: An International Journal of Obstetrics & Gynaecology*, 107(2), 222-227.
10. Bartley, J., & Baird, D. T. (2002). A randomised study of misoprostol and gemeprost in combination with mifepristone for induction of abortion in the second trimester of pregnancy. *BJOG: an international journal of obstetrics and gynaecology*, 109(11), 1290-1294.
  11. Bebbington, M. W., Kent, N., Lim, K., Gagnon, A., Delisle, M. F., Tessier, F., & Wilson, R. D. (2002). A randomized controlled trial comparing two protocols for the use of misoprostol in midtrimester pregnancy termination. *American journal of obstetrics and gynecology*, 187(4), 853-857.
  12. Ziemann, M., Fong, S. K., Benowitz, N. L., Banskter, D., & Darney, P. D. (1997). Absorption kinetics of misoprostol with oral or vaginal administration. *Obstetrics & Gynecology*, 90(1), 88-92.
  13. Yilmaz, B., Kelekci, S., Ertas, I. E., Ozel, M., Sut, N., Mollamahmutoglu, L., & Danisman, N. (2007). Randomized comparison of second trimester pregnancy termination utilizing saline moistened or dry misoprostol. *Archives of Gynecology and Obstetrics*, 276(5), 511-516.
  14. Rose, S. B., Shand, C., & Simmons, A. (2006). Mifepristone-and misoprostol-induced mid-trimester termination of pregnancy: a review of 272 cases. *Australian and New Zealand journal of obstetrics and gynaecology*, 46(6), 479-485.
  15. Vargas, J., & Diedrich, J. (2009). Second-trimester induction of labor. *Clinical obstetrics and gynecology*, 52(2), 188-197.
  16. Jahan, F. S., Ghiyasi, P., & Haghani, H. (2005). Risk factors related to intra uterine fetal death in Iran, A case-control study. *Shiraz E-Medical Journal*, 6(3 & 4).
  17. Abdul, M. A., Shittu, S. O., Ameh, N., & Khan, T. (2006). Effectiveness of misoprostol in the management of intra-uterine foetal death. *Annals of African Medicine*, 5(4), 174-177.
  18. de León, R. G. P., Wing, D., & Fiala, C. (2007). Misoprostol for intrauterine fetal death. *International Journal of Gynecology & Obstetrics*, 99, S190-S193.
  19. EL-Gharib, M. N., & Elebyary, M. T. (2011). Vagiprost in management of second and third trimester intrauterine fetal death. *Medical Practice and Reviews*, 2(2), 16-22.
  20. Nakintu, N. (2001). A comparative study of vaginal misoprostol and intravenous oxytocin for induction of labour in women with intra uterine fetal death in Mulago Hospital, Uganda. *African health sciences*, 1(2), 55-59.
  21. Fawole, A. O., Adekunle, A. O., Sotiloye, O. S., Arowojolu, A. O., & Otolurin, E. O. (2001). Experience with intravaginal misoprostol in the management of intra-uterine fetal death. *Tropical Journal of Obstetrics and Gynaecology*, 18(suppl 1), 35.
  22. Ezechi, O. C., Njokanna, F. O., & Nwokoro, C. A. (2001). Safety and efficacy of misoprostol in induction of labor. *Tropical Journal of Obstetrics and Gynaecology*, 18(suppl.1), 61.