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# Efficacy of misoprostol alone for second trimester termination

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**Abstract**
Misoprostol is a synthetic prostaglandin E1 analog that is initially used for the prevention of peptic and gastric ulcers and now an important drug for women's reproductive health. The main objective is to find out the efficacy and safety of misoprostol in the second trimester to reduce the induction – abortion interval considerably with the lowest possible posology and reduced adverse reactions. A total of 30 patients were enrolled for second trimester termination for various reasons including anomalous baby, contraceptive failures. All the subjects were received a single dose of misoprostol whose posology ranged from 400 to 2000µg intravaginally and was monitored to assess the outcome measures and side effects. Successful termination was possible to all the cases but induction to expulsion time varied from 4 to 21 hours and the maximum termination cases were between 14 and 16 hours (10 cases/ 33.3%). Only six subjects were experienced with side effects like fever, shivering, nausea, vomiting and diarrhea. As a conclusion, due to lesser side effects, non-surgical termination, lesser anxiety and reduced days of hospital stay, misoprostol at single drug is a safe, cost effective and high efficacious drug for second trimester termination.

**Keywords:** Misoprostol, pregnancy termination, lesser side effects

## 1. Introduction
Medical methods of induced abortion have become the bastion in the management of second trimester pregnancy termination (STT) [1, 2]. STT is an important component of comprehensive womens' health care and there are so many reasons for seeking termination including medical and social reasons. Poverty, lower education level, pre-marital pregnancy and having multiple disruptive life events, have been associated with higher rates of seeking STT [3]. Additionally, anatomic or genetic anomalies may also be the reason for nearly 95% of women who choose to terminate their pregnancies [4, 5, 6].

The drug, misoprostol is very much useful for both first and second trimester termination of pregnancy [7, 8, 9]. All the routes of administration including sublingual, buccal, vaginal and rectal are readily absorbed. But the pharmacokinetics of intracervical misoprostol for medical abortion is found scanty [10]. Naturally, the vascularity of the cervix is dense, thus intracervical administration could potentially allow for better absorption of the drug than other route of administration [11].

This drug induces cervical softening and dilation, uterine contractions at all gestational agers thereby facilitating uterine evacuation [12]. The drug potential varied depends on age, route of administration, posology and posological intervals and cumulative dosage [13]. Also, it was found for better local drug action. Thus the overall dosage of the drug and its side effects is reduced [14]. For STT, the dual-therapeutic effect of mifepristone and misoprostol seems to have the highest and the shortest time interval of termination. In monotherapeutic principles, misoprostol alone is considered as the good alternative [15, 16].

Misoprostol using in the STT of pregnancy is clinically as effective and less cost when comparing with other drugs like Gemeprost, Mifepristone, etc. [17] The optimal regimen for STT is the administration of the misoprostol (400µg) vaginally for every 3 to 6 hours [18]. The diarrhea and other gastrointestinal disorders are observed as side effects when more than 800 µg of misoprostol is administered [13].

Visceral reports highlighted the importance of vaginal administration of multiple doses of 800µg of misoprostol [19, 20, 21, 22] and maximum of three doses whereas the oral route is less effective [23, 24]. The sublingual route is a reasonable alternative and may be used as second choice. Alternative routes may be sought as some acceptability studies,

have shown that women prefer a non-vaginal route [25, 26]. The main advantage of the vaginal route is to remove or clean the fragments of the tablets may remain visible for many hours. This study is aimed to determine the shorter induction delivery interval of intravaginal administration of misoprostol in the management of second trimester pregnancy termination.

## 2. Material and Methods

This is a retrospective observational study which was undertaken in the department of Obstetrics and Gynecology, Trichy SRM Medical College Hospital and Research Centre, Tiruchirapalli, India from 2017 to 2018. The institutional ethical committee approval was obtained and around 30 patients were included from outpatient department and labor room having gestational age of 12 to 20 weeks. Before staring the procedure, the patients were counseled properly and written informed consent was obtained.

Ultrasonographic details were collected along with the socio-demographic, clinical history and other necessary examinations. Irrespective of age, marital status and parity, all the patients included were induced with 800µg misoprostol in the posterior fornix of the vagina. Intravenous antibiotics are administered on admission to all patients after instilling vaginal misoprostol. A dosage of 400µg of misoprostol was given at 4$^{th}$ hourly interval for maximum of 4 doses. Anti D immunoglobulin was administered to all Ph negative patients at the time of induction.

Patients who are known allergic or having history of allergic reactions to prostaglandin ($PGE_1$), renal disease, hepatic disorders, cardiac illnesses, severe anemia and maternal coagulopathy are excluded from the study. The indication for seeking STT in general are keeping in mind and interviewed the patients and recorded including congenital abnormalities of the fetus as described by the clinician, failure in contraception, having small child or already having enough child, low socio-economic status and unmarried individuals.

After admission, all the patients were subjected to appropriate laboratory investigations. The appropriate date and time of the induction of the first and consequent doses of misoprostol were noted. The expulsion time also recorded and induction – expulsion inter time were also noted. The painful uterine contraction and side effects were observed and recorded.

## 3. Results

This retrospective study was conducted in 30 patients seeking STT. Each patient was induced with 800µg of vaginal misoprostol in the posterior fornix of vagina and repeated at 4 hours interval. The maximum number of patients was observed between the age group of 21 and 25 years (36.7%). The detailed age group descriptions of the patients included in this study were analyzed and depicted in the table 1.

**Table 1:** Age-wise distribution of the patients (n=30)

| Age group (in years) | No. of patients (n=30) | Percentage |
|---|---|---|
| 17 - 20 | 7 | 23.3 |
| 21 - 25 | 11 | 36.7 |
| 26 - 30 | 6 | 20 |
| 31 - 35 | 5 | 16.7 |
| Above 35 | 1 | 3.3 |

Patients with rural background accounted very high with 86.7% of the total cases while 13.3 % only belonged to urban community. This is mainly because of the situation of the study centre at rural area, so it is convenient for the women belonging to the rural set up to come and get treatment. Majority of the patients included in this study belonged to lower and lower middle socioeconomic classes (15; 50%), followed by middle class (9; 30%), upper middle class (4; 13.3%) and upper class (2; 6.7%).

Maximum subjects were studied only upto primary school (13; 43.3%), followed by collegiate education (6; 20%), upto X and XII of 4 (13.3%) and 4 (13.3%) respectively and illiterate (3; 10%). While distributing the cases according to the parity, we had the record of maximum of multigravida with 13 cases (43.3%) (Table 2).

**Table 2:** Distribution of cases according to the parity

| Parity | No. of patients (n=30) | Percentage |
|---|---|---|
| 0 | 13 | 43.3 |
| 1 | 1 | 3.3 |
| 2 | 6 | 20 |
| 3 | 2 | 6.7 |
| 4 | 5 | 16.7 |
| 5 | 2 | 6.7 |
| >5 | 1 | 3.3 |

Among the patients seeking STT, the common indication was low socioeconomic status and inability to rear another child (36.7%) followed by congenital anomalies (23.3%), etc. (Figure 1). Nearly 17 subjects (56.7%) were of 12 to 16 weeks of gestation and majority of them (15 cases; 88.2%) who sought for STT had a gestation of 16 weeks and 13 cases (43.3%) had gestation between 17 and 21 weeks (Figure 2).

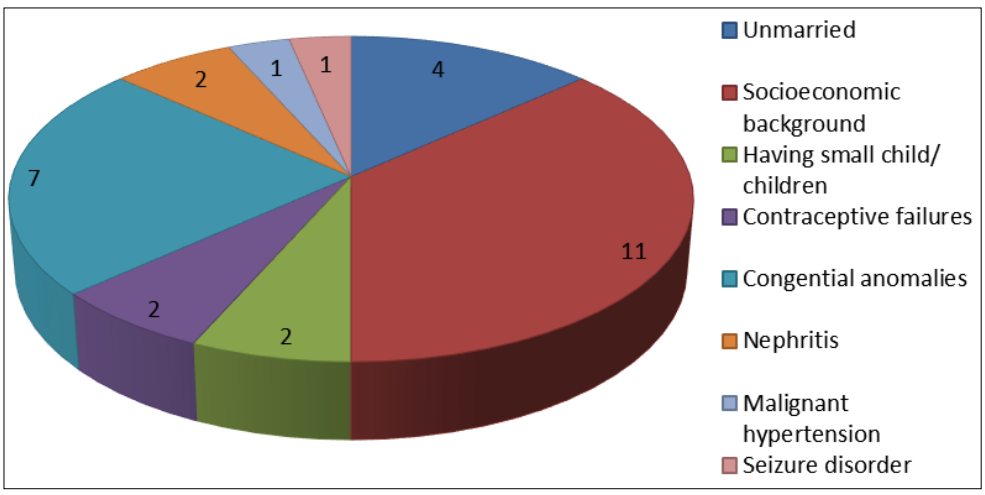


**Fig 1:** Distribution according to the reasons seeking for abortion

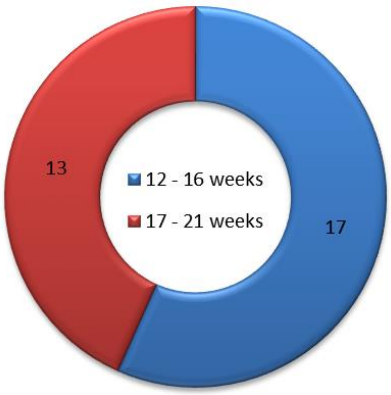


**Fig 2:** Distribution of cases according to the gestation period (in weeks)

The units of misoprostol (posology) was also well analyzed thereby maximum number of cases were found in the gestational week of 16 (15 cases; 50%) followed by 20th week (5 cases; 16.7%). The dosages of the misoprostol got varied among the gestational weeks and patients' age and clinical complications but there is no much correlation was found among the criterias. When gestational weeks increased then the dosage of administration of the misoprostol also get increased. The detailed analysis of gestational weeks, dosage of misoprostol and number of patients received were impregnated in table 3.

**Table 3:** Distribution of gestational weeks and dosage of misoprostol administered

| Gestational Weeks | No. of patients (n = 30) verses units of misoprostol (in µg) administered | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 400 | 800 | 1000 | 1200 | 1400 | 1600 | 1800 | 2000 | 4800 |
| 12 (n=1) | - | - | - | - | - | 1 | - | - | - |
| 15 (n=1) | - | 1 | - | - | - | - | - | - | - |
| 16 (n=15) | 1 | - | - | 6 | - | 4 | - | 4 | - |
| 17 (n=3) | - | - | - | 1 | - | - | 1 | 1 | - |
| 18 (n=2) | - | - | 1 | - | - | 1 | - | - | - |
| 19 (n=2) | - | - | - | 1 | 1 | - | - | - | - |
| 20 (n=5) | - | 1 | 1 | - | - | 2 | - | 1 | - |
| 21 (n=1) | - | - | - | - | - | - | - | - | 1 |

Overall the introduction of vaginal misoprostol in all gestation week groups was found 100% successful. Patients between 12 and 16 weeks of gestation were terminated maximum within 11 to 15 hours followed by 6 to 10 hours at the same situation; patients with 17 to 21 gestational weeks have maximum expulsion time between 16 to 20 hours. The detailed description of the induction – expulsion interval (I-E interval) was depicted in table 4. This indicated of the gestational weeks increased the expulsion time also get increased.

**Table 4:** Distribution of induction – expulsion (I-E) interval by vaginal misoprostol

| I-E time interval (in hours) | No. of cases (n=30) | Gestational weeks verses I-E interval | |
|---|---|---|---|
| | | 12 – 16 weeks | 17 – 21 weeks |
| 0 - 5 | 2 (6.7) | 1 (50) | 1 (50) |
| 6 - 10 | 10 (33.3) | 6 (60) | 4 (40) |
| 11 - 15 | 10 (33.3) | 8 (80) | 2 (20) |
| 16 - 20 | 7 (23.3) | 1 (14.3) | 6 (85.7) |
| 21 - 25 | 1 (3.4) | - | 1 (100) |

[Figure in parenthesis denoted percentages]

The incidence of side effects of misoprostol also observed and well analyzed thereby fever was observed among maximum cases (16.7%) followed by headache (13.3%), abdominal cramp (10%) and diarrhea (10%). It was observed that when the dosage of misoprostol increased the adverse effects like fever, nausea and diarrhea reported. Among the 30 cases, only one received blood transfusion. The reported side effects are shown in table 5.

**Table 5:** Incidence of side effects of misoprostol administration

| Side effects | No. of subjects (n= 30) | Percentage |
|---|---|---|
| Abdominal cramp | 3 | 10 |
| Bleeding | 2 | 6.7 |
| Blood transfusion | 1 | 3.3 |
| Diarrhoea | 3 | 10 |
| Fever | 5 | 16.7 |
| Headache | 4 | 13.3 |
| Nausea/ vomiting | 2 | 6.7 |
| Shivering | 2 | 6.7 |

The questionnaire related to satisfactory status about the method of treatment was interviewed and the data suggested that most of the subjects were satisfied and had some sort of fear in pain and retained products etc. Also they were all ready to utilize the same type of treatment if any forthcoming issues and also ready to recommend to others because they feel this method is safe, cost effective, lesser hospitalization, reduced anxiety, etc. (Table 6).

**Table 6:** Study subjects – questionnaire analysis

| Question | No. of subjects responded (n=30) | | |
|---|---|---|---|
| | Satisfactory | Unsatisfactory | No comments |
| About the method | 27 (90) | 2 (6.7) | 1 (3.3) |
| About the drug | 28 (93.3) | - | 2 (6.7) |
| Avoidance of surgery | 29 (96.7) | - | 1 (3.3) |
| Discretion | 23 (76.7) | 2 (6.7) | 5 (16.7) |
| Less emotional load | 19 (63.3) | 7 (23.3) | 4 (13.3) |
| Tolerance of pain | 12 (40) | 12 (40) | 6 (20) |
| Anxiety about retained tissues | 7 (23.3) | 20 (66.7) | 3 (10) |
| Choose this method again | 28 (93.3) | 1 (3.3) | 1 (3.3) |
| Recommendation of this method | 28 (93.3) | 1 (3.3) | 1 (3.3) |

[Figure in parenthesis denoted percentage]

## 4. Discussion

This study implicated the usage of low-dose misoprostol is highly effective and acceptable as a self-administered abortifacient. The major advantages of the usage of lower and moderate doses of misoprostol are reduced costs and lesser side effects [13, 27]. There were no significant differences among any age groups of the women regarding the determination of safety and efficacy of misoprostol; but some studies suggested that when age of the patient increased, then the side effects also increased (unknown mechanism) [4, 11, 28, 29].

The social stigma related to abortion is still in India, thereby the women cannot come forward independently for pregnancy termination. The family is found to be the responsible factor in dominating or deciding the need of pregnancy or termination. In this study also most of patients informed that the family members induced her to do the termination. Availability of the health care centre in urban areas may help the women to decide in earlier and correct stage to terminate the pregnancy; but the rural women is mostly in dilemma and post termination care is found substantial [6, 28, 29, 30].

The major factors that are influencing and disturbing the termination process for the individual are age, age at sexual activity onset, emotional/ sentimental, educational background, income issues, religion, occupation, fear about abortion procedure, availability of appropriate health care, cooperation of the family, location of abortion, types of treatment, post abortion care and other ethical and legal issues [14, 31, 32].

Many studies suggested that the parity is a major factor that influencing the success of medical termination of pregnancy. A greater parity of the patients was closely associated with a lower efficacy of treatment [31, 32, 33]. In this study the response rate of primigravidae is better than multigravidae which was already reported [34].

The major reasons for the termination of the pregnancy were also well analyzed in this study thereby socioeconomic status dominated (36.7%) followed by congenital abnormalities (23.3%), unmarried (13.3%), etc. Other studies highlighted the reasons as wants to postpone, space between the children, want no more children, socioeconomic status, partner related reasons, too young, working women – so no one to take care of the child, risk of maternal health and risk to fetal health [35, 36].

In this study, the gestational weeks were determined thereby 17 patients were in between 12 and 16 weeks and 13 patients were in between 17 and 21 weeks. In general, it was recorded that the increased gestational age develops risk in abortion and also develop postabortion complications [37, 38, 39, 40]. But in this study, no patients developed any such complications.

In Misoprostol of 400µg for every 3 hours upto 5 doses are mainly used in various health care setups and the same regimen was used in this study [13, 22, 41, 42]. Studies have shown that the additional use of mifepristone shortens the induction–abortion interval and reduces the amount of drug required for the abortion; but the non-availability of mifepristone, only misoprostol is the best alternative. Comparing with oral, vaginal misoprotol showed effective for the induction of abortion [43, 44]; thus the same is followed in this study.

## 5. Conclusion

Our present study confirms the importance and efficacy of misoprostol as the drug of choice for STT. The unsafe abortion is one of the greatest neglected healthcare problems in India and more so in rural India, where lack of education and freely available quality abortion services led to very high maternal mortality and morbidity. Overall the male members of the family need to be educated regarding the contraception and safe abortion, because the causes of unsafe abortion are rooted in a complex set of socio-demographic circumstances. Prompt and early diagnosis of any septic complications and prompt referral to tertiary centres would avoid serious consequences and will save many lives and limit morbidities. Although law, policy and women's right are central to this issue, making abortions safe is above all a public health responsibility of governments.

## 6. References


1. Berghella V, Airoldi J, O'Neill AM, Einhorn K, Hoffman M. Misoprostol for second trimester pregnancy termination in women with prior caesarean: a systematic review. British Journal of Obstetrics and Gynecology. 2009; 116:1151-1157.
2. Kapp N, Borgatta L, Stubblefield P, Vraqovic O, Moreno N. Mifepristone in second-trimester medical abortion. Obstetrics and Gynecology. 2007; 110:1304-1310.
3. Jones RK, Finer LB. Who has second-trimester abortions in the United States? Contraception. 2012; 85:544-551.
4. Anderson N, Boswell O, Duff G. Prenatal sonography for the detection of fetal anomalies: results of a prospective study and comparison with prior series. American Journal of Roentgenology. 1995; 165:943-950.
5. Boyd PA, Devigan C, Khoshnood B, Loane M, Garne E, Dolk H. Survey of prenatal screening policies in Europe for

structural malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. EUROCAT Working Group. British Journal of Obstetrics and Gynecology. 2008; 115:689-696.
6. Shaffer BL, Caughey AB, Norton ME. Variation in the decision to terminate pregnancy in the setting of fetal aneuploidy. Prenatal Diagnosis. 2006; 26:667-671.
7. Ramsey PS, Savage K, Lincoln T, Owen J. Vaginal misoprostol versus concentrated oxytocin and vaginal PGE2 for second-trimester labor induction. Obstetrics and Gynecology. 2004; 104:138-145.
8. Webster D, Penney GC, Templeton A. A comparison of 600 and 200 mg mifepristone prior to second trimester abortion with the prostaglandin misoprostol. British Journal of Obstetrics and Gynecology. 1996; 103:706-709.
9. Ashok PW, Templeton A, Wagaarachchi PT, Flett GMM. Mid trimester medical termination of pregnancy: a review of 1002 consecutive cases. Contraception. 2004; 69:51-58.
10. Rouzi AA, Almansouri N, Sahly N, Alsenani N, Abed H, Darhouse K, Bondagji N. Efficacy of intra-cervical misoprostol in the management of early pregnancy failure. Scientific Reports. 2014; 4:7182.
11. Lalitkumar S, Bygdeman M, Gemzell DK. Mid-trimester induced abortion: a review. Human Reproduction Update. 2007; 13:37-42.
12. Goyal V. Uterine rupture in second-trimester misoprostol-induced abortion after cesarean delivery: a systematic review. Obstetrics and Gynecology. 2009; 113:1117-1122.
13. Tang OS, Gemzell DK, Ho PC. Misoprostol: pharmacokinetic profiles, effects on the uterus and side-effects. International Journal of Gynecology and Obstetrics. 2007; 99:160-168.
14. Desai GS, Chandavarkar A, Gopal S, Sawant G, Desai SV. Second Trimester Medical Termination of Pregnancy with Combined Intracervical and Intravaginal Misoprostol: Comparative Analysis with Intravaginal Misoprostol-A Pilot Study. Journal of Obstetrics and Gynecology India. 2016; 66:157-160.
15. Borgatta L, Kapp N, Society of Family Planning. Clinical guidelines. Labor induction abortion in the second trimester. Contraception. 2011; 84:4-17.
16. Tang J, Kapp N, Dragoman M, de Souza JP. WHO recommendations for misoprostol use for obstetric and gynecologic indications. International Journal of Gynecology and Obstetrics. 2013; 121:186-191.
17. Nor AM, Abdullah HS, Zainul RMR, Jamil MA. Misoprostol (alone) in second trimester terminations of pregnancy: as effective as Geneprost? Journal of Obstetrics and Gynecology. 2006; 26:546-549.
18. Zieman M, Fong SK, Benowitz NL *et al*. Absorption kinetics of misoprostol with oral or vaginal administration. Obstetrics and Gynecology. 1997; 90:88-94.
19. Jain JK, Dutton C, Harwood B, Meckstroth KR, Mishell Jr DR. Aprospective randomized, double-blinded, placebo-controlled trial comparing mifepristone and vaginal misoprostol to vaginal misoprostol alone for elective termination of early pregnancy. Human Reproduction Update. 2002; 17:1477-1482.
20. Carbonell JL. Velazco A, Varela L, Fernández C. The use de misoprostol for termination de early pregnancy. Contraception. 1997; 55:165-168.
21. Jain JK, Harwood B, Meckstroth KR, Mishell JD. Early pregnancy termination with vaginal Misoprostol combined with loperamide and acetominofen prophylaxis. Contraception. 2001; 63:217-221.
22. Velazco A, Varela L, Tanda R, Sanchez C, Barambio S, Chami S *et al*. Misoprostol for abortion up to 9 weeks' gestation in adolescents. European Journal of Contraception and Reproductive Health Care. 2000; 5:227-233.
23. Gemzell DK, Bygdeman M, Aronsson A. Studies on uterine contractility following mifepristone and various routes of misoprostol. Contraception. 2006; 74:31-35.
24. Blanchard K, Shochet T, Coyaji K, Ngoc NTN, Winikoff B. Misoprostol alone for early abortion: an evaluation of seven potential regimens. Contraception. 2005; 72:91-97.
25. Tang OS, Miao BY, Lee SWH, Ho PC. Pilot Study on the use of repeated doses of sub-lingual misoprostol in termination of pregnancy up to 12 weeks gestation: efficacy and acceptability. Human Reproduction. 2002; 17:654-658.
26. Arvidsson C, Hellborg M, Gemzell DK. Preference and acceptability of oral versus vaginal administration of misoprostol in medical abortion with mifepristone. European Journal of Obstetrics and Gynecology Reproduction Biology. 2005; 123:87-91.
27. Schaff EA, Eisinger SH, Stadalius LS, Franks P, Gore BZ, Poppema S. Low dose mifepristone 200mg and vaginal misoprostol for abortion. Contraception. 1999; 59:1-6.
28. Faucher P, Baunot N, Madelenat P. The efficacy and acceptability of mifepristone medical abortion with home administration misoprostol provided by private providers linked with the hospital: a prospective study of 433 patients. Gynecology Obstetrics and Fertility. 2005; 33:220-227.
29. Hajri S, Raifman S, Gerdts C, Baum S, Foster DG. 'This Is Real Misery': Experiences of Women Denied Legal Abortion in Tunisia. PLoS One. 2015; 10:e0145338.
30. Kirti I, Sharad I. Improving access to safe abortion in a rural primary care setting in India: experience of a service delivery intervention. Reproductive Health. 2016; 13:54-59.
31. Monica F, Kristien M, Calsos A, Peter D. Factors influencing abortion decision making processes among young women. International Journal of Environmental Research and Public Health. 2018; 15:329-334.
32. O'Donnell J, Goldberg A, Lieberman E, Betancourt T. I wouldn't even know where to start: unwanted pregnancy and abortion decision making in Central Appalachia. Reproductive Health Matters. 2018; 26:151-158.
33. Philippe L, Martine C, Nicole M, Gerard N. The role of parity in medical abortion up to 49 days of amenorrhoea, The European Journal of Contraception and Reproductive Health Care. 2008; 13:404-411.
34. Agarwal S, Mehdi ZS. Mid-trimester abortions by intra-amniotic prostaglandin. Journal of Obstetrics and Gynecology India. 1976; 14:508-513.
35. Sophia C, Sheila D, Marjorie C, Gilda S. Reasons why women have induced abortions: a synthesis of finding form 14 countries. Contraception. 2017a; 96:233-241.
36. Sophia C, Sheila D, Marjorie C, Sedgh G, Singh S. Characteristics of women obtaining induced abortions in selected low-and middle- income countries. PLoS One. 2017b:12:e0172976.
37. Ekaterine P, Nino L, Nino B, Lia U, Tamar A, Babill SP. Effects of gestational age and the mode of surgical abortion on postabortion hemorrhage and fever: evidence from population based reproductive health survey in Georgia. BMC Women's Health. 2017; 17:136-142.
38. Ferris LE, McMain-Klein M, Colodny N, Fellows GF, Lamont J. Factors associated with immediate abortion

complications. Canadian Medical Association Journal. 1996; 154:1677-1685.
39. Tietze C, Levit S. Legal abortions: early medical complications. An interim report of the Joint Program for the Study of Abortion. Family Planning Perspectives. 1971; 3:6-14.
40. Moberg P, Sjoberg B, Wiqvist N. The hazards of vacuum aspiration in late first trimester abortions. Acta Obstetrics and Gynecology Scandian. 1975; 54:113-118.
41. Wong KS, Ngai CSW, Yeo ELK, Tang LCH, Ho PC. A comparison of two regimens of intravaginal misoprostol for termination of second trimester pregnancy: a randomized comparative trial. Human Reproduction. 2000; 15:709-712.
42. Dickinson JE, Evans SF. The optimization of intravaginal misoprostol dosing schedules in second-trimester pregnancy termination. American Journal of Obstetrics and Gynecology. 2002; 186:470-474.
43. Ho PC, Ngai SW, Liu KL, Wong GCY, Lee SWH. Vaginal misoprostol compared with oral misoprostol in termination of second-trimester pregnancy. Obstetrics and Gynecology. 1997; 90:735-738.
44. Nigam A, Singh VK, Prakash A. Vaginal vs. oral misoprostol formid-trimester abortion. International Journal of Gynecology and Obstetrics. 2006; 92:270-271.