ORIGINAL RESEARCH ARTICLE

Determinants of induction-to-expulsion time and adverse maternal outcomes of second trimester medical abortion in Amhara Region, Ethiopia: Prospective follow-up study

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Abstract

Second-trimester medical abortion (STMA) accounts for 20–40% of abortions in Ethiopia and is associated with risks including uterine rupture, hemorrhage, infection, incomplete abortion, and prolonged hospitalization. This multicenter prospective study included 617 women undergoing STMA in three referral hospitals in the Amhara region from January to October 2024. Induction-to-expulsion time and associated factors were analyzed using Cox proportional hazard modeling. Median fetal and placental expulsion times were 10 and 10.5 hours, respectively, with an 81.2% complete expulsion rate. Prolonged expulsion was associated with higher gestational age, wider misoprostol dosing intervals, and younger maternal age. Reported complications included vaginal bleeding (34.8%), pain (44%), diarrhea (24.1%), vomiting (24%), fever (11.5%), infection (2.4%), incomplete abortion (19.8%), cervical tear (0.49%), and uterine rupture (0.16%). optimizing misoprostol regimens, improving pain management, strengthening follow-up, and ensuring surgical readiness are essential to enhance STMA safety and effectiveness. *(Afr J Reprod Health 2025; 29 [9s]: 162-180).*

Keywords: Abortion interval; Complications; Maternal morbidity; Misoprostol; Safe abortion care

Résumé

L'avortement médicamenteux au deuxième trimestre (AMT) représente 20 à 40 % des avortements en Éthiopie et est associé à des risques tels que la rupture utérine, l'hémorragie, l'infection, l'avortement incomplet et l'hospitalisation prolongée. Cette étude prospective multicentrique a inclus 617 femmes ayant subi un AMT dans trois hôpitaux de référence de la région d'Amhara, de janvier à octobre 2024. Le délai entre le déclenchement et l'expulsion et les facteurs associés ont été analysés à l'aide d'un modèle à risques proportionnels de Cox. Les durées médianes d'expulsion fœtale et placentaire étaient respectivement de 10 et 10,5 heures, avec un taux d'expulsion complète de 81,2 %. Une expulsion prolongée était associée à un âge gestationnel plus élevé, à des intervalles plus espacés entre les prises de misoprostol et à un âge maternel plus jeune. Les complications signalées comprenaient des saignements vaginaux (34,8 %), des douleurs (44 %), des diarrhées (24,1 %), des vomissements (24 %), de la fièvre (11,5 %), une infection (2,4 %), un avortement incomplet (19,8 %), une déchirure cervicale (0,49 %) et une rupture utérine (0,16 %). L'optimisation des schémas posologiques à base de misoprostol, l'amélioration de la prise en charge de la douleur, le renforcement du suivi et la préparation chirurgicale sont essentiels pour améliorer la sécurité et l'efficacité de l'avortement médicamenteux. *(Afr J Reprod Health 2025; 29 [9s]: 162-180).*

Mots-clés: Intervalle entre les avortements, Complications, Morbidité maternelle, Misoprostol, Soins d'avortement médicalisé

Introduction

Abortion is the termination of pregnancy before fetal viability, which is defined as less than 20 weeks of gestation or a fetal weight under 500 g in developed nations, while Ethiopia defines it as below 28 weeks or a fetal weight under 1000 g. Second-trimester medical abortion (STMA), is the termination of pregnancy between 13 and 28 weeks with medication[1-4]. Globally, from 2015-2019,

about 73.3 million abortions occurred annually, of which 45 % was unsafe. The rest 55% was considered safe and 49% of these were carried out in developing countries such as Ethiopia[3-7]. Of these, 10–15% was second-trimester procedures, a period linked to substantial maternal mortality and morbidity, even if the abortion is carried out in a health facility, particularly in low-resource settings[1,3,4,7-10].

Ethiopia has a higher rate of second-trimester medical abortion (STMA), estimated at 20–40%, compared to countries like Kenya (up to 34%), India and South Africa (25–30%), England and Wales (8.6%), and Nigeria (10%)[11-16]. Although STMA is performed in healthcare settings, it carries significant risks and complications. In fact, it disproportionately contributes for two-thirds of major abortion-related complications and poses greater risks compared to first-trimester abortion. Cervical tears or laceration, heavy bleeding, infection, uterine perforation, incomplete abortion, shock, maternal near-miss events, and even death, alongside potential psychological trauma, are some of the adverse events caused by STMA[19,22,23].

One of the reasons for the significant complications associated with STMA, even when performed in a health facility, is the time required to achieve complete expulsion of the pregnancy[4,24]. The process typically involves administering mifepristone followed by misoprostol to induce uterine contractions, which can take longer in the second trimester compared to earlier stages[4, 24-26]. This extended duration increases the risk of complications, including excessive bleeding, infection, and incomplete abortion, as the uterus takes more time and effort to expel the larger fetal and placental tissue. Prolonged exposure to these stressors intensifies the likelihood of adverse events, such as cervical lacerations or uterine rupture, especially in cases where follow-up care is delayed[27]. Evidence underscores the need for timely and skilled management of STMA to minimize these risks while also addressing logistical barriers that could prolong treatment or recovery[28,29].

Ethiopia has adopted the WHO's standard guidelines for second-trimester medical abortion (STMA), but there is limited research assessing their effectiveness, particularly regarding the timing of complete expulsion and adverse maternal outcomes. Research is needed to determine optimal administration routes and reduce procedure duration to improve women's experiences and minimize healthcare burdens[31]. Hence, the current study was designed to determine the time from the first dose of misoprostol to complete expulsion in STMA and the factors affecting it.

The induction-to-expulsion interval for second-trimester medical abortion (STMA) varies globally based on protocols, medications, and healthcare settings. Systematic reviews showed a median interval ranging from 7 to 12 hours with WHO-recommended regimens, influenced by factors like gestational age and parity, interval of misoprostol administration, dose and many other factors[31-33].

For instance, studies reported median induction-to-abortion times of 9.5±2.5 hours in Armenia[34], 7.3 hours in California, USA[35], and 6–9 hours in the UK using mifepristone and misoprostol regimens[36]. A Chinese study comparing 1-day and 2-day mifepristone-misoprostol intervals showed intervals of 7.0±3.0 and 6.8±4.3 hours, respectively[35,37], while a South African study reported a median expulsion time of 8.0 hours[27]. Additionally, a randomized controlled trial using mifepristone followed by misoprostol or oxytocin found a mean induction-to-expulsion interval of 7.0±4.9 hours in the mifepristone- misoprostol group[38]. These findings emphasize the variability in abortion times influenced by location and treatment protocols.

In Ethiopia, the time interval from induction to complete expulsion has not previously been studied but the proportion of cases with complete expulsion has been studied in different part of the country. Some of which include a study at SPHMMC in Addis Ababa, Ethiopia, which found that women undergoing STMA completing expulsion within 24 hours was 81.7%, increasing to 92.5% by 48 hours [39]. In contrast a study at Jimma University reported that 76.6% of women undergoing STMA had complete abortions without complication, but failed to specifically mention the time required to achieve this expulsion rate[19]. Worldwide, using the current recommended regimen, fetal and placental expulsion rate range from 81–94% within 24 hours and 90–97% by 48

hours. When misoprostol is administered continuously without a cutoff, 99% of women eventually achieve a successful abortion, demonstrating the regimen's efficacy and reliability[4,24,39-43].

STMA is a multifaceted procedure where clinical and demographic factors significantly affect the time from induction to expulsion. Identifying these factors is essential to refine protocols and enhance patient care.

The mifepristone-misoprostol combination is highly effective for STMA, significantly reducing the induction-to-expulsion interval compared to misoprostol alone[4,24,32,39,44]. Studies demonstrated that the addition of mifepristone not only enhances uterine responsiveness but also decreases the duration of expulsion. For example, Studies in developed countries, such as the UK, have reported induction-to-abortion intervals as short as 6–9 hours when mifepristone is paired with misoprostol[35]. A systematic review reported median induction times ranging from 7 to 12 hours with the WHO-recommended regimens, emphasizing the effectiveness of mifepristone in reducing expulsion time[31-33].

The dosage and route of misoprostol administration play a significant role in STMA. Vaginal, sublingual, and buccal routes have shown higher efficacy and shorter induction intervals compared to oral administration[29,45,46]. Frequent dosing of misoprostol, such as every 3 hours, is associated with reduced time to expulsion[30,47-49]. The timing between mifepristone and misoprostol administration also significantly affects the induction-to-expulsion interval. Shortening the interval from 24–48 hours to less than 24 hours has been shown to maintain safety and efficacy while potentially reducing the total time for abortion[30,40,47-49].

Gestational age is a critical determinant of induction-to-expulsion time in STMA[27,33,50]. Advanced gestational ages typically require longer intervals due to the increased size of the uterus and volume of fetal tissue, whereas earlier gestational ages, with smaller fetal and placental masses, facilitate quicker expulsion[27,33,42,43,50]. Studies highlight significantly shorter intervals for pregnancies at 13–16 weeks compared to those beyond 20 weeks[42]. Additionally, nulliparous women often experience longer induction times than multiparous women, likely due to differences in uterine responsiveness and prior cervical dilation[27,33,42,43].

Other additional factors such as IUFD, BMI, and previous CD can influence the duration of the induction process. IUFD tends to shorten the expulsion interval, whereas obesity and a history of CD may prolong it due to altered uterine contractility and scarring[5,20,23,27,42,51-55]. Moreover, the disparities in the healthcare environment, including the availability of medication, trained providers, supportive infrastructure, patient monitoring and protocol adherence impacts the induction to expulsion process. Delayed or infrequent monitoring in low-resource settings further contribute to these regional disparities and may prolong the induction-to-expulsion interval and increase the risk of complications[5,20,23,27,42,51-55]. STMA is associated with a range of adverse maternal outcomes, the magnitude of which varies based on clinical protocols, patient factors, clinical factors like gestational age, early recognition, presence of skilled professional, healthcare quality and settings.

Recent studies revealed vaginal bleeding as a common complication in STMA, with reported rates varying from 1% to 20%[6,17,21,28,34,35,40,46,49-51]. Incomplete abortion rate had varied magnitude in different literatures and it occurs in 10-76% of cases, necessitating surgical intervention, and infections or sepsis are reported in 0.1–5% of STMA cases[17,19,27,34,51,53,56]. Cervical injuries occur in 0.5–3% of cases[17,19,27,34,51,53,56]. Although rare (incidence <0.1%), uterine rupture is another severe complication. STMA can lead to emotional distress, particularly when associated with intrauterine fetal demise or fetal anomalies[57,58]. Additional adverse events associated with STMA include nausea and vomiting (28-30%), diarrhea (8-18%), Chills and rigors (14-30%), fever ≥38 °C (14-24%) and seizure is also reported[27,37,42,56].

Several studies in Ethiopia have attempted to evaluate adverse maternal outcomes associated with second-trimester medical abortion. However, most of these studies focus on composite maternal outcomes rather than examining individual complications. Despite global advancements in medical abortion protocols, evidence gaps persist in

Ethiopia, particularly regarding expulsion times, efficacy, and adverse maternal outcomes. Ethiopian studies have also been constrained by small sample sizes and often focusing on composite outcomes. This large, multi-center, prospective study was designed to address these gaps by evaluating induction-to-expulsion intervals, identifying associated factors, and assessing maternal outcomes, ultimately providing critical data to enhance patient care and inform policy.

Methods

Study setting and period

The study was conducted in three selected referral hospitals in Amhara regional state: University of Gondar Comprehensive Specialized referral hospital, Dessie referral hospital, and Tibebe-Gion comprehensive specialized referral hospital. University of Gondar Comprehensive Specialized referral hospital, which serves approximately 13 million people, is located in the historic city of Gondar, Northwestern Ethiopia, at about 12°03′N latitude and 37°28′E longitude, approximately 663 km from the capital, Addis Ababa. Tibebe-Gion Comprehensive Specialized referral Hospital is located in the capital city of Amhara region, Bahir Dar, 497 km northwest of Addis Ababa, at 11°36′N latitude and 37°23′E longitude. Dessie Referral Hospital, which serves a population of 10 million, is located in the South Wollo Zone, Dessie city. It is situated at latitude of 11°8′N and a longitude of 39°38′E, approximately 400 km from Addis Ababa. The study was conducted from January to October 2024. Gestational age was calculated using reliable LMP or ultrasound milestone done until 23W6D.

Study design

Multicenter prospective study design was conducted to determine the time from the first dose of misoprostol to the complete expulsion of all products of conception, assess associated factors and maternal adverse events of STMA in three referral hospitals in the Amhara region, Ethiopia, in 2024 G.C.

Source population: All pregnant women who came for abortion care at the three-referral hospital in Amhara regional state.

Study population: All pregnant women who underwent STMA at the three referral hospitals in the Amhara Regional State who met the eligibility criteria during data collection from January to October 2024.

Eligibility criteria: All pregnant women who come for second trimester induced medical abortion care in the study period were included, whereas those who had contraction at presentation and/or rupture of membranes; cervical osmotic dilators placed or balloon catheter used for cervical ripening were excluded from the study.

Sample size determination: Since we had both categorical and continuous outcome variables to measure the effectiveness of misoprostol, the sample size was calculated using formulas for a single population mean and a single population proportion. The larger estimate, 632, was selected to maximize the statistical power of the study.

Sampling technique: We used consecutive sampling technique to include all pregnant women who came for second trimester induced medical abortion care at the three referral hospitals until the final sample size was attained.

Data collection tool: A pretested and structured interviewer administered questionnaire was prepared using Kobo toolbox electronic data collection tool. It was prepared in English and later translated to Amharic language which makes things easy to be under stood by data collectors (midwives and/or residents) as well as the patients. The questionnaire was pretested at Michu Clinic of one General Hospital in the Amhara Region by the data collectors, a month before the study to establish the suitability, practicability and reliability of the study questions. Modifications and adjustments to the questioner were made as appropriate.

Data collection procedures and data quality control: The principal investigator and supervisors recruited two research assistants per site and trained them on data collection procedures, including the use of structured questionnaires, patient recruitment, and obtaining consent. Six research assistants collected data, introducing themselves to eligible patients and obtaining consent before

administering questionnaires. Data covered socio-demographic characteristics, past obstetric history, medical conditions, and current pregnancy details. Patients were then followed for one-week post-discharge to assess delayed or late complications. Data from questionnaires were supplemented by patient files and direct information from patients. Supervisors and the investigator ensured data quality by supervising collectors and reviewing questionnaires daily.

Data Analysis: Collected data were checked for completeness while it was in the Kobo Toolbox before being exported, which was then exported to STATA version 17 for further cleaning and coding. Descriptive analysis focused on induction-to-expulsion time and maternal complications was done. Kaplan-Meier survival analysis was used to estimate the baseline mean and median expulsion times, with the first complete expulsion treated as a failure event and subsequent data censored.

Patients were monitored for seven days post-misoprostol administration and those requiring surgical intervention for non-expulsion were documented as censored cases. A Cox proportional hazard model identified factors influencing time to expulsion, with variables having a p-value ≤ 0.20 in the bivariate analysis included in the multivariable model. Results were reported using Adjusted Hazard Ratios (AHR).

Study variables

Dependent variable

Time from first dose of misoprostol to expulsion of all product of conception

Secondary outcomes: Hemorrhage (vaginal bleeding), incomplete abortion, surgical uterine evacuation, uterine perforation/rupture, Pain requiring analgesics, uterine infection/sepsis, Death of the woman, Seizure, Psychological trauma.

Independent variables

Socio -demographic factors: Age, Religion, Place of residence, Marital status, Occupation, Educational status, BMI, Service availability
Obstetric factors: Gestational age, Gravidity, Parity, Previous uterine scar, Previous abortion, Previous ectopic pregnancy
Fetal factors: Fetal heartbeat, Fetal anomaly, Fetal presentation
Medication: Drugs given for abortion and dose, Duration from mifepristone to misoprostol administration, Route of misoprostol administration, Dosing interval of misoprostol

Operational definitions

Complete abortion: The whole product of conception is expelled, the uterus is small, empty on U/S and well contracted, scant vaginal bleeding, and only mild cramping.
Event: complete expulsion of the fetus and placenta with medications administered
Time to expulsion or survival time: The time interval between the administration of the initial misoprostol dose and the complete expulsion of the fetus and placenta for those having the event (complete expulsion). Time was recorded in munities for the purpose of accuracy and then converted to hour during analysis and interpretation.
Vaginal bleeding: Bleeding that occurred after the initiation of medication for abortion. It was documented based on the clinician's estimation of the blood loss.
Surgical intervention: a surgical procedure done to complete the abortion process. It includes manual removal, MVA, cervical tear repair, vaginal tear repair or uterine repair or hysterectomy.
Pain score: pain is scored out of 10 in our study and the following table provides the pain score description
Anemia - hematocrit <33% or HGB<11gm/dl

Mild Pain: Characterized by nagging or annoying sensations that do not significantly interfere with daily activities	**Moderate Pain**: Significantly interferes with daily living activities and concentration.	**Severe Pain**: Disabling pain that dominates attention and prevents daily functioning.
1: Barely noticeable pain often ignored.	1: Moderate pain that can be temporarily ignored during focused activities but remains distracting.	1: Severe pain limiting activities and social interactions, often disrupting sleep
2: Minor and annoying pain, with occasional stronger sensations	2: Moderately strong pain, difficult to ignore, but some work or social activities are still manageable with effort	2: Intense pain, restricting physical activity and making conversation arduous
3: Noticeable and distracting pain, but adaptable over time	3: Pain that disrupts normal activities and concentration	3: Excruciating pain, with uncontrolled vocalization or moaning, unable to communicate effectively 4: Unbearable, potentially delirious pain that confines the patient to bed

Maternal death: – death of pregnant women due to abortion and its complication after admission to the hospital and one week within discharge.

Pelvic infection or sepsis: is a uterine infection, occurring during, or shortly after the abortion process due to bacterial contamination. Diagnosis is made using fever> 38.0^{o}celcius , which may progress to shock and one or more of the following symptoms, including foul-smelling vaginal discharge, rapid heart rate, severe abdominal pain, cervical motion tenderness, gross hematuria, flank pain, oligo-anuria and/or using laboratory criteria on CBC (leukocytosis with/without left shift or elevated Creatinine.

Shock: BP < 90/60 mmHg

Failed medication abortion: failure to achieve complete fetal and placental expulsion despite continued misoprostol administration and/or need of surgical intervention to complete the abortion process

Adverse maternal outcome: a patient undergoing STMA and developing one of the following complications including chills, pain, diarrhea, fever, blood loss, shock, need of transfusion, anemia, surgical uterine evacuation, uterine rupture, pelvic infection, death of the woman or seizure.

Ethical considerations

Ethical approval was obtained on 26th December 2023 from the CMHS/SH Institutional Ethical Review board office on behalf of the Institutional Review Board (IRB) of University of Gondar with reference number of R/T/T/C/Eng/165/26/2023. Following this, formal permission to conduct the study was secured from the administration of TGCSRH, DRH, UoGCSRH, and the heads of the Department of Gynecology and Obstetrics of each referral hospitals. The data were collected after written informed consent had been obtained from study participant and conducted according to the principles expressed in the declaration of Helsinki. Personal identifiers were not used on the data collection proforma to ensure confidentiality of the study participants.

Results

Socio-demographic and reproductive characteristics

A total of 617 women who came for STMA were included in the study from January to October 2024. University of Gondar Comprehensive Specialized Referral Hospital (UoGCSRH) contributed the largest share, with 236 participants (38.2%), followed by Dessie Referral Hospital (DRH) with 194 participants (31.4%) and Tibebe-Gion Comprehensive Specialized referral Hospital (TGCSRH) with the remaining 187 participants (30.3%). The majority of women seeking STMA were aged 20-29 (56.2%); primigravida (42.63%) or have had 2-4 pregnancies (45.7%), and nearly half (49.1%) were nulliparous. (Table 1)

Table 1: Reproductive characteristics of women seeking medication abortion services

Reproductive traits and history	Variable category	Frequency	Percentage (%)
Gravidity	Primigravida	263	42.63
	Multigravida (II-IV)	282	45.70
	Multigravida(V-VI)	54	8.75
	Multigravida (VII and above)	18	2.92
Parity	Nulliparous	303	49.10
	Parous (I)	125	20.30
	Multiparous (II-IV)	167	27.10
	Multiparous (V-VI)	18	2.90
	Multiparous (VII and above)	4	0.60
Previous cesarean uterine scar	No	575	93.20
	Yes	42	6.80
Number of cesarean uterine scars	1	32	76.19
	2	7	16.67
(N=42 out of 617 = 6.80 %)	>=3	3	7.14
Other type of uterine scare	No	615	99.68
	Yes	2	0.32
Previous abortion	No	503	81.52
	Yes	114	18.48
Number of previous abortions	One abortion	81	71.05
	Two abortion	20	17.54
	More than two	13	11.40
Pervious ectopic pregnancy	No	611	99.03
	Yes	6	0.97

Table 2: Condition of the current pregnancy

Condition of the current pregnancy	Category	Frequency	Percent (%)
GA by ultrasound	14-17+6 week	236	38.2
	18 - 23+6 week	266	43.1
	24 – 27+6 week	115	18.6
What was the reason for abortion?	Rape	134	21.72
	Incest	32	5.19
	Continuance of the pregnancy endangers maternal/fetal health	16	2.59
	Unable to bring up the child, owing to her status a minor or a physical infirmity	7	1.13
	Obstetric indication	188	30.47
	2nd trimester fetal demise	187	30.30
	Other reasons	53	8.59
Other reasons for abortion	Lack of support / money or inadequate income to raise a child	15	28.30
	Disagreement with partner or husband	37	69.81
	Trauma related indication	1	1.89
Presentation of the fetus for GA> 25 week, N=78	Cephalic	61	78.21
	Breech	17	21.79
Mean GA by US	19 weeks+5 days ± (4 weeks = Std. D)	Minimum = 14 weeks, Max = 27 week + 6 days	

Table 3: Conditions of current abortion

Conditions of current abortion	Category		Frequency	(%)
Drugs given for abortion	Mifepristone alone		1	0.16
	Mifepristone then misoprostol		565	91.57
	Misoprostol alone		51	8.27
Duration from mifepristone to misoprostol administration in hrs [n=565]	< 6 hrs.	<2 hrs.	75	13.27
		2-5.99 hrs.	9	1.59
	6-12 hrs.		50	8.85
	12.1-24hrs		229	40.53
	24.1-48 hrs.		157	27.79
	48.1-72hrs		33	5.84
	>72 hrs.		12	2.12
Time Interval of Misoprostol Administration (in Minutes)	180		338	54.8
	240		259	42.0
	330		1	0.2
	360		19	3.1
Route of administration	Vaginal		124	20.10
	Sublingual		295	47.81
	Vaginal then sublingual		193	31.28
	Oral		5	0.81
Complete Medical abortion	No		117	18.8
	Yes		501	81.2
Fetus expelled by medical abortion	No		2	0.30
	Yes		615	99.7
Was the Placenta expelled with Medical abortion?	No		116	18.80
	Yes		501	81.20
Preparation of misoprostol used	200 mcg		604	97.9
	50 mcg		13	2.1
Total number of Misoprostol dose in grams?	< or = 400 mcg		83	13.5
	401-800		165	26.7
	8001-1200		143	23.2
	1201-1600		95	15.4
	1601-2000		52	8.4
	2001-2400		28	4.5
	2401-2800		15	2.4
	2801-3200		13	2.1
	>/= 3201		23	3.8
How many doses of misoprostol was the patient given?	1		47	7.62
	2		159	25.77
	3		141	22.85
	4		100	16.21
	5		56	9.08
	6		39	6.32
	>/= 7		75	12.15
Time to both fetal and placental expulsion with 12 hours interval	<12 hrs.		292	58.2
	12-23.99 hrs.		146	29.1
	24-35.99 hrs.		39	7.8
	36-47.99 hrs.		13	2.6
	>/= 48 hrs.		12	2.4
Post abortion Hct. Determined?	Yes		187	30.31
	No		430	69.69
Misoprostol dose (µg)	Mean 1340.92 ± 912.69 (Std. D)		Median = 1200 Range = 6250	Min=150 Max=6400
Time to fetal expulsion (hrs.)	Mean 12.9147 ± 11.34 (Std. D)		Median =10 Range = 89.67	Min = 1.00 Max = 90.67
Time to placental expulsion (hrs.)	Mean -13.5511 ± 11.79 (Std. D)		Median 10.5 Range=90	Min = 1.00 Max = 91.00
What was the level of hematocrit after abortion? N=187 (30.31%)	Mean ➔ 33.25 ± 5.86 (Std. D)			

Condition of the current pregnancy and abortion process

The majority of women (67.75%) did not know their last menstrual period (LMP), though 100% underwent ultrasound for gestational age (GA) confirmation. (Table 2)

Combination of mifepristone and misoprostol was used in 91.57% of cases (47.81%-sublingual misoprostol and most common mifepristone-to-misoprostol interval was 12.1–24 hours-40.53%). Fetal expulsion occurred in 99.7%, with a median time of 10 hours (mean 12.91 ± 11.34 hours) and median time to both fetal and placental expulsion was10.5 hours (mean 13.55 ± 11.79 hours). Complete fetal and placenta expulsion was achieved in 81.2%, with 87.3% completing within 24 hours and only 2.4% taking longer than 48 hours. (Table 3)

Complications due to misoprostol administration

Misoprostol administration was associated with several complications. Fever (11.5%), vomiting and diarrhea (24% each), chills (44.2%), pain (78.9% with varying intensity: mild-7.8%, moderate-27.1%, severe-27.2%, and excruciating-16.9%), vaginal bleeding (34.8%, amount wise from 151–300 ml-47%, >750 ml-2.3%) and pelvic infection-2.4%. Surgical interventions were required in 23.18% of cases, predominantly MVA-18.8, cervical tear repair and uterine rupture repair. (Table 4)

Follow-Up Checkups

Only 6.8% of returned for checkups; the rest were contacted via phone call interview. Hematocrit testing was performed in 7.1% of cases, revealing anemia (Hct <33%) in 59.1% of those tested. Symptomatic bleeding or anemia affected 6.5% of patients.

Predictors of time to expulsion of STMA

Bi-variable analysis and multivariable cox regression on factors associated with time to Expulsion

Bi-variable Analysis

In this study, variables that met the Cox regression assumptions were included in the bi-variable analysis. Older age was associated with a shorter time to complete expulsion, with those aged 30-34 years showing a hazard ratio (CHR) of 1.247 (95% CI: 1.030–1.510) and those aged ≥35 years showed a CHR of 1.386 (95% CI: 1.106–1.735). Higher parity and gravidity were associated with slightly faster expulsion times (CHR = 1.07, 95% CI: 1.018–1.131, and CHR = 1.08, 95% CI: 1.030–1.133, respectively). A one-week increase in gestational age was associated with a 6.4% longer time to expulsion (CHR = 0.936, 95% CI: 0.914–0.959). Longer durations between mifepristone and misoprostol administration increased the time to expulsion (CHR = 0.995, 95% CI: 0.991–0.999). Higher total doses of misoprostol were also associated with prolonged expulsion time (CHR = 0.999, 95% CI: 0.999–0.9994). A 6-hour misoprostol interval significantly delayed expulsion compared to the 3-hour and 4-hour intervals (CHR = 0.528, 95% CI: 0.330–0.846). Women undergoing abortion for socioeconomic reasons (CHR = 5.45, 95% CI: 3.89–7.62) or due to fetal demise (CHR = 1.29, 95% CI: 1.01–1.64) had faster expulsion, possibly due to previous abortion or delivery experience. Additionally, the sublingual (CHR = 0.739, 95% CI: 0.585–0.933) and mixed (vaginal followed by sublingual) routes (CHR = 0.753, 95% CI: 0.586–0.968) of misoprostol administration significantly prolonged expulsion time compared to the vaginal route. (Figure 1)

Multivariable analysis

In this study, variables satisfying the cox CHX2 assumption were fitted in to the bi-variable. From bi-variable analysis age, parity, gravidity, number of alive children, gestational age, interval between mifepristone and misoprostol administration, total doses of misoprostol, misoprostol administration interval, dose of misoprostol at each dosing, reasons for abortion, route of misoprostol administration, marital status and previous Abortion were significantly associated to time of expulsion and were having p-value of 0.2 or less and included in the multivariable analysis.

Younger women (<30 years) had longer expulsion times, with those aged 20-24 years (AHR = 0.811,

Table 4: Complication due to misoprostol administration

Complication	Category	Frequency	Percentage
Fever due to misoprostol administration	No	546	88.5
	Yes	71	11.5
No of fever records	1 record	20	28.17
	2 records	32	45.07
	3 records	16	22.54
	>/= 4 records	3	4.23
Vomiting >2 episodes	No	469	76.0
	Yes	148	24.0
Chills due to Misoprostol	No	344	55.8
	Yes	273	44.2
Pain due to Misoprostol administration	No	130	21.1
	Yes	487	78.9
Diarrhea due to Misoprostol	No	468	75.9
	Yes	149	24.1
Vaginal bleeding due to abortion process by misoprostol	No	402	65.2
	Yes	215	34.8
Shock due to medical abortion	No	211	34.20
	Yes	4	0.60
Transfusion of blood products	No	207	96.30
	Yes	8	3.70
Was surgical uterine intervention needed?	No	484	76.82
	Yes	143	23.18
What was the surgical intervention needed	MVA	123	18.8
	E&C or D&C	3	0.49
	Cervical tear repair	3	0.49
	Manual placenta removal	3	0.49
	Uterine repair	1	0.16
	Trans-cervical balloon catheter	10	1.62
Was there pelvic infection during or after the abortion process?	No	602	97.6
	Yes	15	2.4

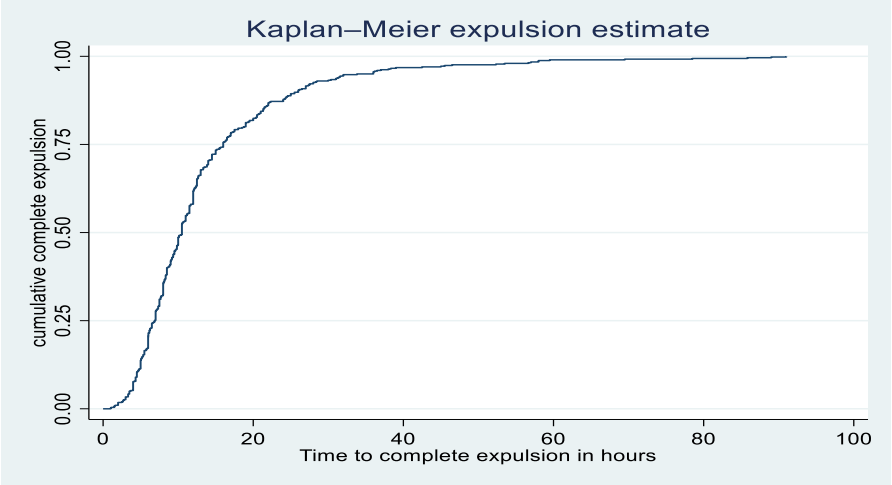

Figure 1: Kaplan-Meier survival functions for time (in hours) to complete expulsion of product of conception.

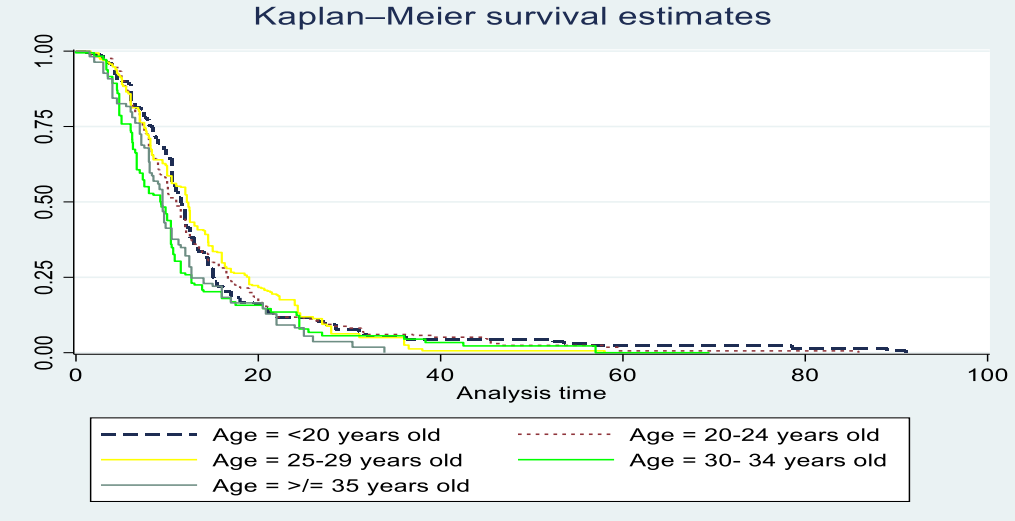

Figure 2: Kaplan-Meier survival estimates for time to complete expulsion Vs Age

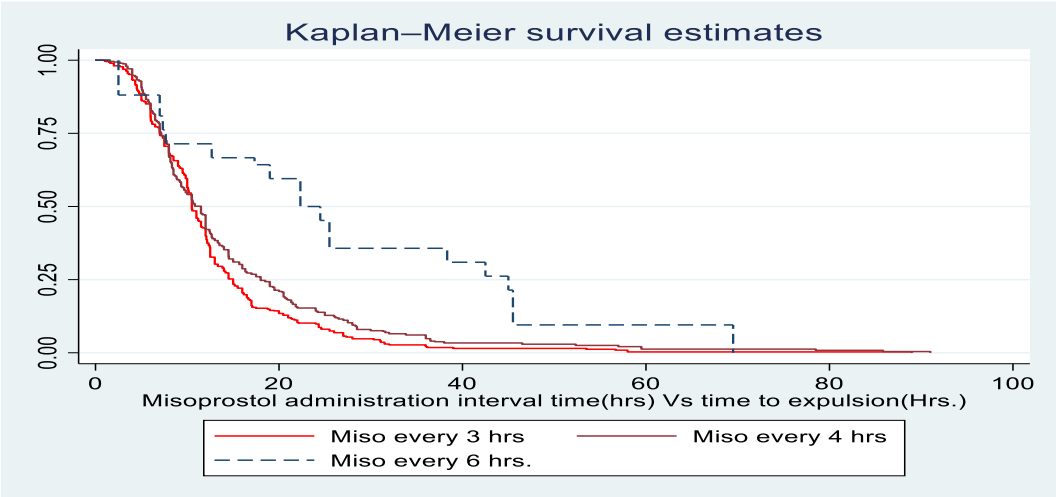

Figure 3: Kaplan-Meier survival estimates for time to complete expulsion Vs Interval of Misoprostol

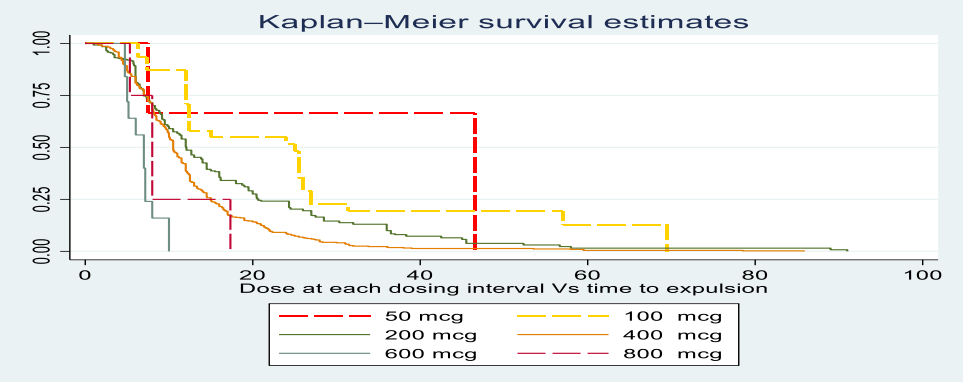

Figure 4: Kaplan-Meier survival estimates for time to complete expulsion Vs Dose at each dosing interval for misoprostol

Table 5: Bi-variable and multivariable cox regression analysis of time to complete fetal and placental expulsion

Variable Name	Expulsion Yes (N=501, 81.2%)	Crud HR [95% CI]	AHR [95% CI]
Age of the patient			
<20 years old	100(84.03)	1.00	1.00
20-24 years old	143(82.65)	1.047[0.890, 1.233]	0.811[0.671, 0.980] *
25-29 years old	130(74.71)	1.009[0.855, 1.189]	0.710[0.574, 0.877] *
30- 34 years old	77(84.61)	1.247[1.030, 1.510] *	0.702[0.514, 1.000]
>/= 35 years old	51(85)	1.386 [1.106,1.735] *	0.9134[0.638, 1.306]
Parity		1.073 [1.017, 1.132] *	0.875 [0.594, 1.288]
Gravidity		1.080[1.029, 1.133] *	1.1731[0.949, 1.448]
Alive Children		1.065[1.008, 1.125] *	1.034[0.715, 1.495]
GA from Ultrasound		0.936 [0.914, 0.959] *	0.926[0.904, 0.951] *
Mifepristone to Misoprostol interval		0.995 [0.991, 0.999] *	1.004[1.0001,1.0092]*
Total Gram of Misoprostol		0.999[0.99912,0.9999] *	0.9987[0.9985,0.999]*
Dose of Misoprostol at Each Dosing		1.0019[1.0010,1.0027] *	1.0053[1.0042,1.006]*
Marital Status			
Single	128(86.48)	1.00	1.00
Married	364(79.82)	1.334[1.172, 1.520] *	0.881[0.649, 1.139]
Divorced or widowed	10(76.92)	2.914[1.867, 4.546] *	1.065[0.627, 1.802]
Previous Abortion			
No	19(16.67)	1.00	1.00
Yes	95(83.33)	1.310[1.046, 1.641] *	0.765[0.513, 1.140]
Interval Between Doses of Misoprostol			
3 hours	264(78.1)	1.00	1.00
4 hours	218(84.17)	0.847[0.707, 1.014]	0.711[0.584, 0.867] *
6 hours	19(95)	0.529[0.330, 0.846] *	0.248[0.139, 0.443] *
Reason for Abortion			
Pregnancy as a result of sexual assault (reference)	143(86.14)	1.00	1.00
Maternal or Fetal Indication for Termination	170(83.33)	1.143[0.913, 1.431]	1.141[0.721, 1.805]
Socioeconomic Reason for Abortion	55(91.66)	5.446[3.890, 7.623] *	3.629[2.189, 6.020] *
Fetal Demise	133(71.12)	1.287[1.013, 1.636] *	1.025[0.643, 1.634]
Route of Misoprostol administration			
Vaginal route	106(85.48)	1.00	1.00
Sublingual route	249(83)	0.739[0.585, 0.933] *	1.043[0.798, 1.362]
Mixed vaginal then sublingual route	146(75.64)	0.753[0.586, 0.968] *	0.939[0.718, 1.226]

***CHR** =Crude hazard Ratio **AHR=** Adjusted hazard Ratio, 95% CI=Confidence Interval ***p-value<0.05, ** p-value <0.001,** 1.00= reference group*

95% CI: 0.671-0.980) and 25-29 years (AHR = 0.710, 95% CI: 0.574-0.877) showing prolonged times. Increased gestational age also significantly delayed expulsion (AHR = 0.926, 95% CI: 0.904-0.951). Longer intervals between mifepristone and misoprostol slightly increased expulsion likelihood (AHR = 1.004, 95% CI: 1.0001-1.0092), while higher doses of misoprostol at each interval reduced expulsion time (AHR = 1.0053, 95% CI: 1.0042-1.0064). Higher total misoprostol doses were associated with prolonged time to expulsion (AHR = 0.999, 95% CI: 0.9986-0.9999). Among dose intervals, a 4-hours interval had slowed expulsion compared to 3-hours (AHR = 0.711, 95% CI: 0.584-0.867), and a 6-hours interval further delayed it significantly (AHR = 0.248, 95% CI: 0.139-0.443). Socioeconomic reasons for abortion were associated with faster expulsion (AHR = 3.63, 95% CI: 2.19-6.02), potentially due to prior abortion or delivery experiences. Parity, gravidity, number of

children, marital status, previous abortion history, and route of misoprostol administration were not significantly associated with expulsion time. (Table 5)

Discussion

In this study, the median time to fetal expulsion was 10 hours (mean: 12.91 ± 11.34 hours), and the median time to placental expulsion was 10.5 hours (mean: 13.55 ± 11.79 hours). The complete expulsion rate was 81.2%. A significant delay in expulsion was observed with increasing gestational age (GA), 7.4% increment for each additional week in the GA (AHR = 0.926, 95% CI: 0.904–0.951). Longer intervals between mifepristone and misoprostol administration (>48 hours) were associated with slightly prolonged expulsion times (AOR = 1.004, 95% CI: 1.0001–1.0092). Increased interval between misoprostol doses from 3 to 4 hours delayed expulsion by 29.89 % (AHR = 0.711, 95% CI: 0.584–0.867), with a 6-hour interval causing significant delays (65.2%) (AHR = 0.248, 95% CI: 0.139–0.443). Increasing the dose at each interval showed reduced expulsion time (AHR = 1.0053, 95% CI: 1.0042-1.0064). Younger women (<30 years) experienced longer expulsion times, particularly those aged 20–24 years (AHR = 0.811, 95% CI: 0.671–0.980) and 25–29 years (AHR = 0.710, 95% CI: 0.574–0.877).

The findings on the fetal and placental expulsion time align with studies conducted in Armenia (median: 9.5 ± 2.5 hours)[34], Uzbekistan and Ukraine (15h)[60], University of Southern California (12 hours)[61], Stanford University, Stanford, CA, USA(9.3-12.9 h)[62] and Boston University (10 hours). The similarity may stem from comparable protocols used for pregnancy termination across these studies. However, the expulsion time observed in our study are slightly longer than those reported in USA (7.3 hours)[35], UK (6–9 hours) [36], Israel (7.0 ± 4.9 hours)[38], South Africa (8.0 hours)[27] and a Chinese study comparing 1-day and 2-day mifepristone-misoprostol intervals (7.0 ± 3.0 and 6.8 ± 4.3 hours, respectively)[37]. These differences may be attributed to strict adherence to standardized protocols and better follow-up in these studies. Additionally variations in misoprostol dosing regimens, interval of misoprostol administration, intervals between mifepristone and misoprostol administration might explain the difference, as some of these studies are experimental randomized controlled trials comparing different dosage regiment and interval of dosing. Further research with alternative study designs and settings is needed to clarify these discrepancies.

As to the complete expulsion rate, which was 81.2% in this study, it is slightly higher than the previous studies done in Jimma University, Ethiopia (76.6%) which could be possibly due to majority of their study participants were unmarried (more than 84%) and has no previous delivery experience and on top of that, intrauterine second trimester fetal demise were not included in their studies[19]. Our study has a slightly lower expulsion rate than the study done in Saint Paul's Hospital Millennium Medical College in Addis Ababa, Ethiopia, (92.5%) which could be due to a higher misoprostol dosage regimen they applied in their setting for GA 24-27+6 weeks, which might improve the expulsion rate[39]. Our finding is also lower than most global studies using the current WHO recommended regimen and ranges from 90-97% expulsion within 48 h[28,31-33,39,43, 44] which might raise the issue of our resource limited setting's strict adherence to the standard recommended misoprostol dose, dosage interval and follow-up as well as logistic availability.

STMA is a multifaceted procedure where clinical and demographic factors significantly affect the time from induction to expulsion. Identifying these factors is essential to refine protocols and enhance patient care. In this study, a significant delay in expulsion was observed with increasing GA, 7.4% increment for each additional week in the GA (AHR = 0.926, 95% CI: 0.904–0.951), consistent with findings from studies in South Africa, Israel and Austria[27,38,43]. These studies demonstrated that shorter abortion times were associated with well-dated pregnancies and lower gestational ages. For instance, a study from Austria in 2020 reported that earlier gestational age was linked to faster abortion completion, underscoring the impact of gestational age on expulsion timing. These findings highlight the importance of promoting early termination of pregnancy in our context. This can be achieved by

increasing awareness among women about the benefits of early intervention, enhancing the healthcare system's capacity for timely identification of fetal anomalies, and addressing the high prevalence of pregnancies resulting from sexual assault. Furthermore, it is crucial to educate young women of reproductive age about their rights to access safe and timely abortion care services.

In our study, longer intervals between mifepristone and misoprostol administration (>48 hours) were associated with slightly prolonged expulsion times (AOR = 1.004, 95% CI: 1.0001–1.0092). This is supported by studies from Stanford University, CA, USA, (62), Vietnam[40] and Shanghai, China,[37] which found that shorter intervals between mifepristone and misoprostol significantly reduced total abortion time while achieving clinically comparable induction times. These findings highlight that cervical ripening with mifepristone is effectively achieved within 48 hours, making extended waiting periods unnecessary. Prolonging the interval beyond this timeframe only increases expulsion time without offering any additional clinical benefit.

Similarly, increasing the interval between misoprostol doses from 3 to 4 hours delayed expulsion by 29.89 % (AHR = 0.711, 95% CI: 0.584–0.867), with a 6-hour interval causing significant delays (65.2%) (AHR = 0.248, 95% CI: 0.139–0.443). These findings are supported by a study in Thailand and systematic review of 29 studies, including 20 randomized controlled trials, which concluded that shortening misoprostol administration interval reduces total abortion time without compromising safety or efficacy[6,33,35,36,47]. This indicates that shorter interval of misoprostol administration has a proven effect to shorten evacuation even though individualization for each patent is imperative.

In our study, increasing the dose at each interval showed reduced expulsion time (AHR = 1.0053, 95% CI: 1.0042-1.0064). Other researches supported this finding, showing that higher doses per interval lead to quicker expulsion. A study in California found that using 400 mcg of misoprostol every 3 h compared to lower doses, either vaginally or sublingually, resulted in shorter induction-to-abortion intervals with similar side effects[60]. Another study in Bursa, Turkey[63] and Vancouver also linked higher doses to faster expulsion and higher success rates. Thus, while higher doses at each interval can expedite expulsion, the overall dose must be carefully balanced to avoid complications.

In this study, younger women (<30 years) experienced longer expulsion times, particularly those aged 20–24 years (AHR = 0.811, 95% CI: 0.671–0.980) and 25–29 years (AHR = 0.710, 95% CI: 0.574–0.877). These findings align with other studies from South Africa, Israel, the USA, Ethiopia, and other countries, which link younger age, nulliparity, and advanced gestational age to prolonged induction-to-abortion intervals[6,27,33,35,36,38,43,47]. Previous delivery or abortion experience appears to significantly reduce expulsion time, likely due to increased uterine sensitivity to misoprostol and quicker cervical ripening in women with such histories.

In our study, vaginal bleeding occurred in 34.8% of patients, with most cases (47%) involving blood loss of 151–300 ml. Higher volumes were recorded as follows: 301–450 ml (21.4%), 451–600 ml (7.9%), 601–750 ml (1.4%), and >750 ml (2.3%). Shock due to medical abortion process was rare, affecting 0.6%. These rates are lower than those reported in other sub-Saharan countries, such as Zambia (44%) and a systematic analysis of 70 studies from 28 countries (57%)[17,64,65]. The discrepancy may be attributed to either under-recording or underestimation of blood loss among the study participants or improvements in STMA care within our setting. Careful interpretation is necessary to fully understand these findings. This is further strengthened by researches done in other parts of Ethiopia, which showed the hemorrhage rate to be 30% with transfusion rate of approximately 2.5%, almost similar to our finding of 3.7%[21,22].

In this study, surgical intervention was required in 23.2% of cases, with Manual Vacuum Aspiration (MVA) being the most common intervention. There was one case of uterine rupture, corresponding to a rate of 0.16%. This finding is comparable to the rate reported in a study from Jimma (23.4%), likely due to similarities in the study population and the misoprostol regimen used[19]. The uterine rupture rate observed in our study is consistent with previously reported rates,

which range from 0.2% to 0.4% in the literature, highlighting the rarity of this complication. However, it also underscores the importance of critical and stringent follow-up for STMA cases, particularly in resource-limited settings like ours, to mitigate risks and ensure patient safety.

In this study, pain was reported by 78.9% of patients and pain intensity was rated on a 10-point scale, with most of the patients (44%) experiencing severe pain (score of >7 out of 10). This finding is significantly higher than the prevalence reported in developed countries, such as Bologna, Italy (38%)[66]. This disparity can be attributed to stricter pain management protocols along with the wider availability of pain control medications in developed nations. These findings highlight the need to incorporate effective pain management into local protocols, ensuring the availability and practicality of appropriate analgesic options to improve patient comfort during medical abortion.

Fever occurred in 11.5% of our study participants, which is notably lower than the 42% reported in the Netherlands [67]. This discrepancy can be attributed to several factors. One possibility is the underestimation and under documentation of fever, which may result from suboptimal follow-up care. Additionally, the Dutch study included both surgically and medically managed cases, spanning both first- and second-trimester pregnancies, which could have introduced variability in the study participants and management protocols. In contrast, our findings are higher than those from developed countries such as Finland, Australia, and Italy, where the prevalence of fever is reported to be extremely low, although exact figures are not always provided[43, 64]. This difference may be due to the more advanced approaches to managing complications like fever and better follow-up care in these developed settings.

In our study, significant vomiting (≥2 episodes) occurred in 24%, while diarrhea affected 24.1% of our study participants.

Pelvic infection was diagnosed in 2.4% of our study participants, which were confirmed through clinical and laboratory findings. This is consistent with findings in other study from Ethiopian, which identified pelvic infection rates of 1.5–3% in similar populations undergoing medical abortion. Globally, pelvic infection rates vary widely depending on abortion protocols, hygiene standards, and follow-up care. For instance, studies from Kenya in 2017 and South Africa in 2020 reported similar infection rates in low-resource settings where access to sterile equipment and follow-up care may be limited. In contrast, high-income countries like Finland and the United States reported lower rates, often below 1%, due to routine use of prophylactic antibiotics, higher procedural sterility, and timely follow-up. These findings underscore the importance of improving infection prevention measures, particularly in low-resource settings, to further reduce the incidence of pelvic infections associated with medical abortion.

Strengths and limitations

This study's multicenter design, large sample size and enhances its generalizability within Ethiopia, while the prospective nature minimizes recall bias. Being referral hospital-based, the study may not fully represent cases managed at primary hospitals or health centers with different resources and expertise. Misclassification bias is possible in assessing complications like bleeding, as estimates relied partly on clinical judgment. Complications may also be underreported due to phone-based follow-up, which can miss late or minor events. The short follow-up period further limits detection of late complications. In addition, the use of consecutive sampling may have introduced selection bias.

Implication for current practice and policy

This study highlights the urgent need to improve the way second-trimester medical abortion (STMA) is provided in Ethiopia. The Ministry of Health could strengthen current guidelines by reducing the waiting time between mifepristone and misoprostol, and by adopting shorter, evidence-based misoprostol dosing schedules. Making safe abortion care available earlier in pregnancy is just as important, since higher gestational age not only delays expulsion but also raises the risk of complications. This will require stronger community awareness and better support for

women to recognize pregnancy early and seek timely care.

At the same time, policies should ensure that women receive adequate pain relief, that facilities are prepared with surgical backup—such as MVA kits, trained providers, and emergency readiness—and that outcomes are consistently monitored through a national reporting system. Finally, this study offers a useful starting point for researchers to explore improved regimens of dose, interval, and route, with the goal of making STMA safer, faster, and more supportive for women in Ethiopia.

Conclusion

This study showed the median time to fetal and placental expulsion was still higher with lower complete expulsion rate. Higher GA, Longer mifepristone- misoprostol intervals (>48 hours), longer interval between misoprostol doses, dose used at each dosing interval and Younger women (<30 years) were significantly associated with time to expulsion.

Misoprostol is a highly effective option for second-trimester abortion in resource-limited settings, demonstrating a high success rate and a relatively short median induction-to-expulsion time. However, longer expulsion times and complications remain challenges, particularly in younger women and at advanced gestational ages. The findings underscore the need to optimize misoprostol regimens, including dose adjustments and interval modifications, especially for late 2nd trimester abortions, to enhance outcomes. Furthermore, improving follow-up care, addressing challenges in abortion services to have early termination of pregnancy, and strengthening pain management strategies, infection prevention, and surgical backup are critical for better patient experiences. Expanding access to early abortion care and conducting further research to refine treatment protocols are essential steps to ensure safer and more effective medical abortion practices in resource-limited settings.

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Authors' contributions

EFY, GSA, and SMA conceived the study and developed the design. EFY, SMA, BSA, and NAA oversaw data entry, completeness, and quality across all sites. EFY, SMA, and AML conducted data coding, cleaning, and analysis. EFY, SMA, BSA, and AML performed the statistical analysis and drafted the initial manuscript. NAA, EFY, MMB, and SMA critically revised the final version. LBT provided mentorship throughout the project, from inception to completion. All authors contributed to data interpretation, manuscript drafting, and approved the final version for submission.

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Data availability

The data are available from the corresponding authors on reasonable request.

Competing interests

The authors declare no competing interests.

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