

**COMPARISON OF EFFICACY OF MISOPROSTOL  
ALONE OVER MIFEPRISTONE AND MISOPROSTOL  
COMBINATION FOR TERMINATION OF  
PREGNANCY FROM 12 TO 20 WEEKS GESTATION:  
A PROSPECTIVE OBSERVATIONAL STUDY**



**A DISSERTATION SUBMITTED TO THE TAMIL NADU DR. M. G. R. MEDICAL  
UNIVERSITY, CHENNAI IN PARTIAL FULFILLMENT OF THE REQUIREMENTS  
FOR THE AWARD OF M.S DEGREE IN OBSTETRICS AND GYNAECOLOGY  
(BRANCH II) EXAMINATION TO BE HELD IN MAY 2022**

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A PROSPECTIVE OBSERVATIONAL STUDY**

Dissertation submitted to the  
THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY,  
CHENNAI

In partial fulfillment of the requirements  
for the degree of MASTER OF  
SURGERY

IN  
OBSTETRICS AND GYNAECOLOGY

By  
SONIA BABY JOHN

Registration Number: 220620500017

DEPARTMENT OF OBSTETRICS  
AND GYNAECOLOGY CHRISTIAN  
MEDICAL COLLEGE, VELLORE

MAY 2022

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MIFEPRISTONE AND MISOPROSTOL COMBINATION FOR TERMINATION  
OF PREGNANCY FROM 12 TO 20 WEEKS GESTATION:  
A PROSPECTIVE OBSERVATIONAL STUDY”**

is the bonafide work of Dr. Sonia Baby John under my supervision in the Department of Obstetrics and Gynaecology, Christian Medical College, Vellore in partial fulfillment of the requirements for the M.S Obstetrics and Gynaecology Examination of the Tamil Nadu Dr. M.G.R Medical University to be held in May 2022 and no part thereof has been submitted for any other degree.

Guide

Dr Swati Rathore,  
Professor, Department of Obstetrics and  
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Christian Medical College,  
Vellore – 632004.

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A PROSPECTIVE OBSERVATIONAL STUDY”**

is the bonafide work of Dr. Sonia Baby John, Post Graduate Student in the Department of Obstetrics and Gynaecology, Christian Medical College, Vellore and is being submitted to The Tamil Nadu Dr. M. G. R Medical University in partial fulfilment of the MS Obstetrics and Gynaecology examination Branch II to be conducted in May 2020 and no part thereof has been submitted for any other degree.

Dr Anna Pulimood,  
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## **DECLARATION**

I, Sonia Baby John, do hereby declare that the dissertation titled “**COMPARISON OF EFFICACY OF MISOPROSTOL ALONE OVER MIFEPRISTONE AND MISOPROSTOL COMBINATION FOR TERMINATION OF PREGNANCY FROM 12 TO 20 WEEKS GESTATION: A PROSPECTIVE OBSERVATIONAL STUDY**” is a genuine record of research done by me under the supervision and guidance of Dr. Swati Rathore, Professor, Department of Obstetrics and Gynaecology, Christian Medical College, Vellore and has not previously formed the basis of award of any degree, diploma, fellowship or other similar title of any university or institution.

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## **ACKNOWLEDGMENTS**

Throughout the writing of this dissertation, I have received a great deal of support and assistance.

I would like to express my sincere gratitude to my guide, Dr. Swati Rathore, Professor of Obstetrics and Gynaecology-Unit V, Christian Medical College and Hospital, whose expertise was invaluable in the formulating of this research topic and methodology in particular. I would also like to thank her for her valuable help, guidance and support in this endeavor.

I would like to thank Dr. Jiji Mathews, Professor and head of department of Obstetrics and Gynaecology, Christian Medical College and Hospital, Vellore, Dr Santhosh Benjamin, Dr Hilda Yenuberi, Dr Richa Sasmita Tirkey for their constant support and encouragement.

My heartfelt gratitude to Mrs. Thenmozhi Mani, department of Bio –statistics and Mr. Madhan, department of CEU, for their help and assistance.

I thank my husband, parents, brother, sister-in-law and friends for their support and sympathetic ear.

Above all I would like to thank Lord Jesus for His strength throughout this endeavor and for helping me to complete this project with success.

# INSTITUTIONAL REVIEW BOARD (IRB) APPROVAL LETTER



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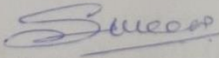
Dear Dr. Sonia Baby John,

I enclose the following documents:-

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Suceena Alexander, Addl. Vice  
Principal (Research), so that the grant money can be released.

With best wishes,

  
Dr. Suceena Alexander  
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Dear Dr. Sonia Baby John,

The Institutional Review Board (**Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled “Comparison of efficacy of Misoprostol alone over Mifepristone and Misoprostol combination for termination of pregnancy from 12 to 20 weeks gestation: A prospective observational study” on October 05, 2020.

The Committee review the Following Documents:

- 1) IRB Application Format
- 2) Patient information sheet and Consent Form (English, Tamil, Telugu)
- 3) Proforma
- 4) Cvs. Of Drs. Santosh, Jiji Mathews, Richa, Hilda, Sonia, Swati R.
- 5) No. of Documents 1 -4.

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on October 05, 2020 in the New IRB Room, Christian Medical College, Vellore 632 004.

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Dr. Premila Abraham	M.Sc. Ph.D	Professor, Department of Biochemistry, CMC, Vellore	Internal Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of Withdrawals for the study entitled: "Comparison of efficacy of Misoprostol alone over Mifepristone and Misoprostol combination for termination of pregnancy from 12 to 20 weeks gestation: A prospective observational study" on a monthly basis. Please send copies of this to the Research Office ([research@cmcvellore.ac.in](mailto:research@cmcvellore.ac.in)).

The Institutional Ethics Committee expects to be informed about the progress of the project, Any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are

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expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: [http://172.16.11.136/Research/IRB\\_Policies.html](http://172.16.11.136/Research/IRB_Policies.html) in the CMC Intranet and in the CMC website link address: <http://www.cmch-vellore.edu/static/research/Index.html>.

Fluid Grant Allocation:

*A sum of Rs 8,000/- INR (Rupees Eight thousand only) will be granted for 12 Months.*

Yours sincerely,

Dr. Suceena Alexander  
Secretary (Ethics Committee)  
Institutional Review Board

Dr. Suceena Alexander, MD., DM., FASN.  
Secretary - (Ethics Committee)  
Institutional Review Board  
Christian Medical College,  
Vellore - 632 002, Tamil Nadu, India.

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## **ABBREVIATIONS**

TOP - Termination of Pregnancy

PGE1 - Prostaglandin E1

NSAIDS - Non-Steroidal Anti-inflammatory Drugs

MTP - Medical Termination of Pregnancy

RCT - Randomized Controlled Trial

WHO - World Health Organization

GOI - Government of India

FOGSI - Federation of Obstetric and Gynaecological Societies of India

ICOG - Indian College of Obstetrics and Gynaecology

RMP - Registered Medical Practitioner

AUC - Area Under Curve

IAI - Induction Abortion Interval



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TERMINATION OF PREGNANCY FROM 12 TO 20 WEEKS  
GESTATION: A PROSPECTIVE OBSERVATIONAL STUDY**

**INTRODUCTION**

Termination of pregnancy is an essential service of reproductive health care and is one of the safest procedures when performed legally under safe guidelines. Among millions of abortions that occur annually worldwide, ten percent occur in the second trimester (1).

“Abortion can be defined as the loss of pregnancy by expulsion or extraction when it is not viable or when it weighs 500gms or less”. Abortions can be either spontaneous or induced. An induced abortion is voluntary termination of pregnancy for various reasons such as lethal fetal anomalies, pregnancy causing risk to life or grave injury to the woman, pregnancy caused by rape or contraceptive failure with presumed grave injury to mental health of the woman as described in the Medical Termination of Pregnancy (MTP) Act, formulated by the Government of India. Recently there has been a gradual increase in number of mid trimester abortions (from 13 to 20 weeks of gestation) one of the reasons being the advancement in prenatal screening of fetal anomalies. Various clinical settings

have shown, miscarriages carried out at later gestations have higher risk of complications, and not only require more time, but also impacts on financial burden. When pregnancy is terminated in the mid-trimester, the morbidity and mortality is much greater than when it is terminated in the first trimester. Complication after second trimester abortions is approximately 0.4 to 0.6% (1). The various modes of medical termination of pregnancy are medical and surgical methods. The latter are associated with increased chances of infection, bleeding requiring transfusion, genital tract injury, uterine perforation/rupture. Also, some medical methods involving prostaglandin preparations result in side effects such as pain, nausea, vomiting, diarrhea and serious cardiorespiratory complications.

In developing countries like India, second trimester termination of pregnancy is still a challenge. Much emphasis has been put on the need to increase effectiveness and decrease complications by adopting safe methods for termination of pregnancy. Traditionally, numerous methods have been used for second-trimester abortion. But the search for the ideal method, that is safe, easily available, cost effective and optimally acceptable is still going on. The World Health Organization (WHO) recommends the various safe options and appropriate pregnancy duration for conducting abortion (2).

After the first trimester, medical termination is usually done as an inpatient procedure. This can be done either medically or surgically. The patient choice and consent is of paramount importance. Skilled health care provider, availability of safe medications and aseptic methods is equally important. Both interventional methods for termination of

pregnancy are safe and effective when provided by skilled, experienced health personnel. European countries have preferred medical methods more commonly whereas dilation and evacuation procedures (D&E) is the more prevalent method in the United States (1).

The frequently used pharmacological regime used for inducing abortion are prostaglandin analogues, such as Misoprostol. The various routes of Misoprostol administration can be oral, sublingual, buccal, and vaginal. The various dose regimens popularly prescribed can be from 200 to 800 mcg. The frequency of usage also varies from every 4 hours, 6 hours, 8 hours and 12 hours.

Misoprostol is easily available, cheap and is commonly used for other obstetric indications like induction of labour, cervical ripening before surgical procedures, prevention and treatment of postpartum hemorrhage.

Misoprostol being the standard agent of second-trimester abortion may be used with or without pretreatment with Mifepristone (an anti-progesterone). Mifepristone binds to the progesterone receptor and prevents progesterone from exerting its action. Research suggests that pretreatment with Mifepristone (also known as RU 486) helps in attaining comparable efficacy with lower doses of Misoprostol, resulting in a shorter induction-to-abortion interval. This approach is based on the evidence that Mifepristone primes the myometrium and cervix for prostaglandin activity and therefore, it aids in the conversion of the quiet pregnant uterus into an organ of spontaneous activity. Mifepristone administration results in degeneration of endometrial decidua, ripening and dilatation of cervix, release of endogenous prostaglandins, and increased sensitivity of the myometrium

to the contractile effects of prostaglandins. The metabolic clearance rate of mifepristone is 0.55 L/kg/day (3). Because of its slow rate of removal from circulation it can be administered in a single oral dose. Mifepristone alone has been found to be less effective, resulting in abortion within 1–2 weeks in 92% to 54% of pregnancies (4).

### **JUSTIFICATION**

In our setting, both the regimes are being followed for termination of second trimester pregnancies depending on the treating clinician's preference. Hence, we did this observational study to compare the efficacy of these two different methods of second trimester termination of pregnancy.

## **AIM AND OBJECTIVES**

**AIM:** To compare the efficacy of misoprostol alone over mifepristone and misoprostol combination for termination of pregnancy from 12 to 20 weeks gestation.

### **PRIMARY OBJECTIVE:**

To compare the induction to abortion interval (IAI) – of the two regimes [Misoprostol alone and Mifepristone plus Misoprostol] used for termination of pregnancy from 12 to 20 weeks gestation.

[IAI - the duration from the first dose of Misoprostol administration to complete expulsion of fetus and placenta]

### **SECONDARY OBJECTIVES:**

1. To determine the maximum dosage and frequency of Misoprostol required for complete abortion from 12 to 20 weeks gestation.
2. To assess the need for surgical evacuation needed after medical termination of pregnancy between 12-20 weeks with these 2 medical regimens.
3. To compare side effects and complications.
4. To compare the cost effectiveness - the impacts of the two regimes in the length of hospital stay and cost of treatment.

## **REVIEW OF LITERATURE**

Although the majority of pregnancy terminations are performed in the first trimester, the rate of second-trimester pregnancy termination is high, which accounts for 10–15 % of abortions worldwide. Terminations are mainly done due to anomalies in the fetus and unplanned/ unwanted pregnancy. While illiteracy and lack of access to contraception and limited clinical services remains a challenge across poor income countries, the advancement of ultrasound technology and medical genetics laboratories in prenatal diagnosis has increased the detection rate of fetal abnormality in mid-pregnancy. Therefore, the incidence of induced abortions in the second-trimester of pregnancy has increased substantially (5).

Worldwide, the estimated rate for induced abortions from 2010 to 2014 was 35 per 1000 women aged 15 to 44 years. The rate in developed countries was 27 per 1000 and in developing countries was 37 per 1000. About 10 to 15 percent of abortions done per year around the world are in the second-trimester of pregnancy (6).

A large number of women are undergoing unsafe abortions and the number is rising. Hence the need for safe abortion by giving proper healthcare facilities is crucial and remains as a major challenge. The estimated maternal deaths worldwide directly due to consequences of unsafe abortions accounts to 300 - 500 per day (7).

WHO (2017) classifies MTP as safe abortions and unsafe abortions. Safe abortion

is defined as “TOP which is done by trained personnel with a WHO recommended method that is appropriate for the gestational age”. The definition of unsafe abortion is “the termination of an unplanned pregnancy by personnel not trained with the required skills or in a set up not having the basic medical facilities or both”. Unsafe abortion is further classified as ‘less safe abortion’ and ‘least safe abortion’. ‘Less safe abortion’ is defined as “one that is done by person with training but he/ she uses an inappropriate technique or one that is done by a safe technique but by a person not trained in doing it”. ‘Least safe abortion’ is “when termination of pregnancy is done by a person not trained and when he/ she uses life threatening techniques or methods which are not safe”. Abortions if not done with caution can lead to complications like excessive bleeding, infection, sepsis and injuries, and is the fourth leading cause of maternal death.

In India, abortion has a major role when it comes to the reproductive health in women (8). Access to safe abortion care and family planning services is an integral component of maternal health care (9). To make abortion safe and accessible to Indian women, guidelines have been developed by GOI, FOGSI and IOCG, which govern all aspects of TOP.

## **The Medical Termination of Pregnancy Act, 1971**

**(An Act which deals with the termination of pregnancies by RMPs)**

The purpose of formulating the Indian Medical Termination of Pregnancy (MTP) Act was for decreasing the number of unsafe abortions. In 1971, the Indian parliament passed the MTP Act and in 1972 it was enforced. It was established by the Ministry of Health and Family Welfare, GOI, with the goal of promoting women's health. The various areas addressed were the importance of legalizing abortions, the need for achieving easy access to health care services for safe abortions and thereby preventing unsafe abortions. The MTP Act allows for willful termination of pregnancy before the fetus is viable for clearly defined indications. These indications are based on therapeutic, eugenic, humanitarian and social grounds. It should be performed by registered medical practitioners in a registered place with proper authorization.

The MTP Act clearly defines:

- Indications for MTP.
- Gestational age at which termination can be performed.
- Persons who are qualified to perform the procedure
- Place of implementation of MTP.
  - Who should give consent.

As per the MTP Act 1971, **pregnancies may be terminated by registered medical**



**practitioners:**

- (a) Pregnancy not more than 12 weeks and 1 RMP gives opinion that -
- (b) Pregnancy more than 12 weeks but not more than twenty weeks and 2 or more RMPs gives opinion in good faith, that -
  - (i) The continuation of the pregnancy would be risky/ life threatening to the woman or can cause grave injury to her health either physically or mentally or
  - (ii) There is a considerable risk of physical or mental problems causing serious handicap in the child if it was born.

The Act also states the following:

- If any pregnancy is caused as a result of rape as alleged by the pregnant woman and the anguish caused by such pregnancy is believed to cause a grave injury to the mental status of the rape victim and also if any pregnancy occurs as a result of contraceptive failure by any married woman or her husband for the purpose family planning, the anguish caused by such unwanted pregnancy is believed to cause a grave injury to the mental status of the pregnant woman.
- Pregnancy termination can be done only with the permission and consent of the mother.
- Pregnancy termination of women less than 18 years or of women more than 18 years but is a lunatic can be terminated only with the consent in writing of her guardian.
- All termination of pregnancy should be conducted in
  - (a) A hospital registered under or maintained by Government, or
  - (b) A setup temporarily being approved for the implementation of this Act by Government

(10).

In 2021, the new MTP Amendment Act 2021 was passed and has come into force. The purpose of the Amendment Act is to make available safe, comprehensive and quality abortion facilities for all women in the country and will help in putting an end to preventable maternal mortality. The progress in medical technology has contributed towards this.

Key amendments:

- In case of rape survivors, incest victims, disabled women and some others, the upper limit of gestation was increased from 20 to 24 weeks.
- The opinion of one RMP is mandatory for MTP up to 20 weeks of gestation. The opinion of two RMPs is needed for MTP from 20-24 weeks of gestation.
- In case of considerable fetal abnormalities, diagnosed and approved by an authorized Medical Board, upper limit of gestation not applicable.
- Confidentiality clause - The name and other details of a woman undergoing MTP cannot be revealed to anyone except to a person authorized by law.
- Failure of contraception made applicable to unmarried women based on her choice irrespective of marital status, to provide access to safe abortion (11).

**Table 1: Difference between MTP Act 1971 and MTP Amendment Act 2021**

	MTP Act 1971	MTP Amendment Act 2021
Contraceptive failure as indication	Applicable only to married women	Applicable to unmarried women also
Gestational age limit	Up to 20 weeks (for all indications)	Up to 24 weeks for rape survivors and beyond 24 weeks for substantial foetal anomalies
Medical practioners opinion before termination	1 RMP up to 12 weeks 2 RMPs up to 20 weeks	1 RMP up to 20 weeks 2 RMPs 20 to 24 weeks Medical board approval after 24 weeks
Breach of woman's confidentiality	Fine up to Rs 1000	Fine and/ or imprisonment of 1 year

## **METHODS OF SECOND TRIMESTER TERMINATION OF PREGNANCY**

Termination of pregnancy can be performed in the second trimester by either medical or surgical methods. Termination of pregnancy in the second trimester is technically more difficult and has higher rate of complications. An ideal method would be one which is safe, quick, 100% effective, inexpensive and without any immediate or late side effects. Since there is no ideal method available at present, a method that is effective with minimal side effects and complications is usually chosen.

The methods used are:

- A) Medical methods
- B) Surgical methods

### **A) MEDICAL METHODS**

Misoprostol

Mifepristone

### **B) SURGICAL**

Dilatation and evacuation

Manual vacuum Aspiration

Dilatation and curettage

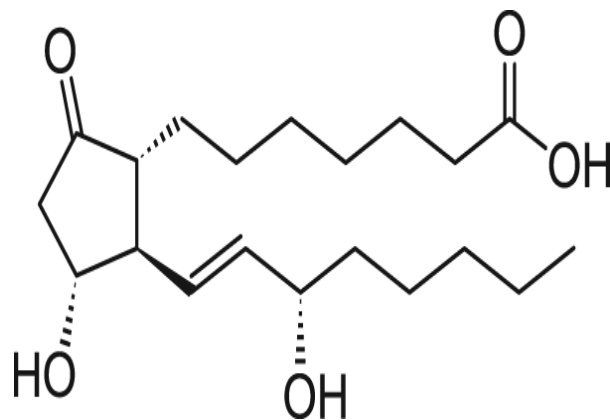
## MEDICAL ABORTION

### MISOPROSTOL

Misoprostol is a synthetic analogue of prostaglandins E1 (15-deoxy-16-hydroxy-16-methyl PGE1) which was developed for prevention of peptic ulcer because of mucosal protective properties (12). It is a cytoprotective prostaglandin. The 'E' in PGE1 refers to the substituent of the pentane ring and the '1' refers to the number of double bonds in the side chain (13).



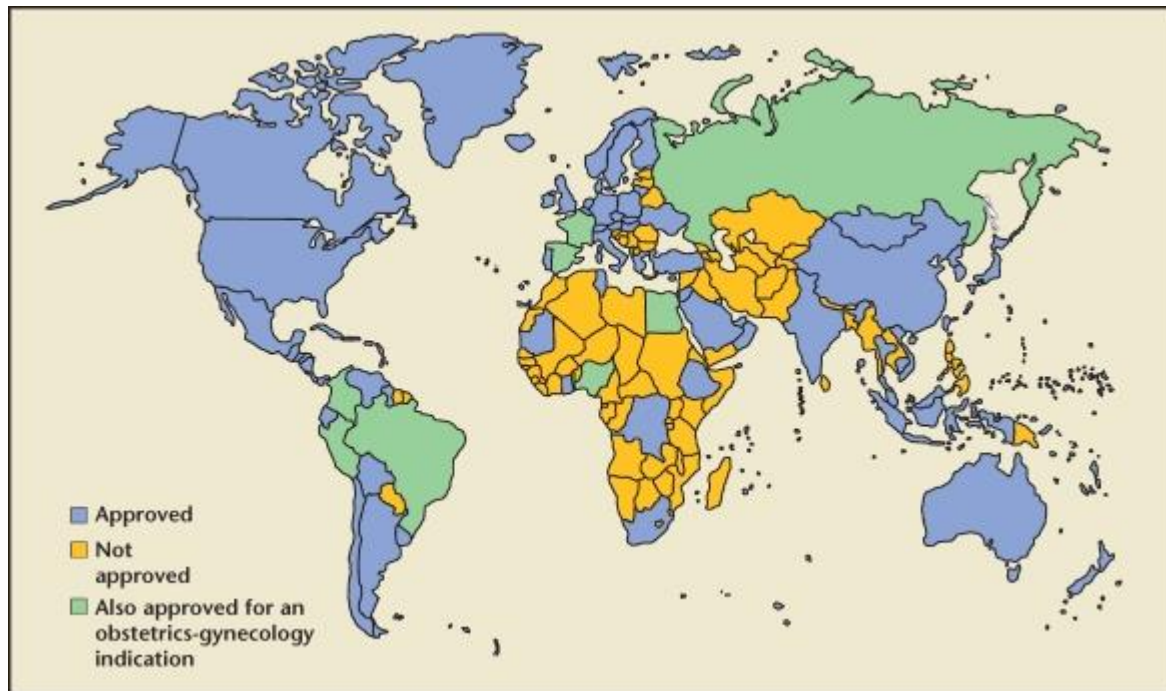
**Figure 1:** Misoprostol 200 mcg tablets(14)



**Figure 2:** Chemical structure of PGE1(15)

Misoprostol was introduced and marketed as an oral agent used in prevention and treatment of gastroduodenal damage induced by nonsteroidal anti-inflammatory drugs (NSAIDs). It is used for a wide range of indications in the field of obstetrics and gynecology including medication termination of pregnancy, medical management of miscarriage, ripening of cervix before surgical procedures, induction of labor and in the treatment of postpartum hemorrhage. However, it is used as an off-label drug in many countries. The US FDA has not allowed Misoprostol for the above-mentioned indications. But in 2002, pregnancy was removed from the label as an absolute contraindication to misoprostol use (16). Misoprostol's effects are dose dependent and include cervical softening and dilation, initiation of uterine contractions. Its side effects include nausea, vomiting, diarrhea, fever, and chills. It can be used per oral, per vaginum and sublingually. This analogue differs from and is better than other analogues of prostaglandin in that it is:

- Inexpensive
- Can be stored at room temperature for long period without change in the efficacy
- Worldwide availability
- Orally active and effective through multiple routes of administration
- Has low rate of dose dependent risk
- Long shelf life



**Figure 3:** World map of misoprostol approval(17)

## Pharmacokinetics

There are various routes of administration of Misoprostol but studies have shown that the most effective route is vaginal and sublingual followed by oral (18). The routes of misoprostol administration can be per oral, S/L, buccal, and per vaginal). The various dose regimens popularly prescribed are from 200 to 800 mcg. The frequency of usage also varies from every 4 hours, 6 hours, 8 hours and 12 hours.

Pharmacokinetics studies have shown that vaginal misoprostol is associated with a greater overall exposure to the drug (area under the curve [AUC]) and improved effects on the cervix and uterus. On comparing oral and vaginal administration, studies

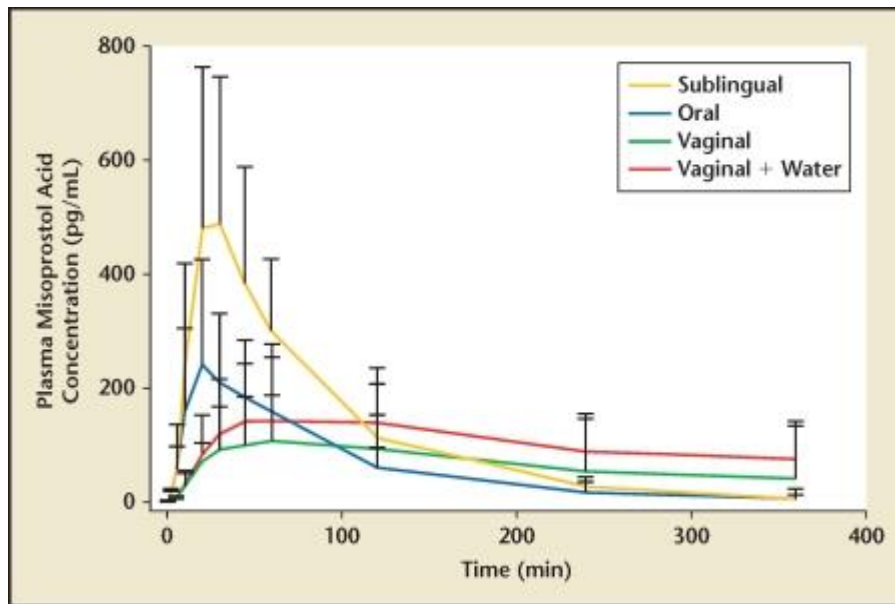
have shown that vaginal misoprostol is absorbed gradually, attains lower peak plasma levels and is also cleared gradually, similar to an extended-release preparations. However, the absorption of misoprostol through the vaginal epithelium among different women is widely varied. There is no clinically significant difference between dry or moistened (with water, saline or acetic acid) administration of vaginal misoprostol (16). Randomized controlled trials have shown better efficacy for complete evacuation with vaginal Misoprostol compared to placebo (80% versus 16% p value <0.01) and lesser need for surgical evacuation (28% versus 84% p value <0.001) (19).

The rectal route and sublingual routes of administration show a similar pattern to vaginal administration. But rectal route has a lower AUC and a significantly lower maximum peak concentration. Whereas, sublingual route of administration has more rapid absorption and higher peak levels than either vaginal or oral administration (Figure 4) which explains higher rates of gastrointestinal side effects. Despite this, the sublingual route causes uterine contractions at a rate equivalent to vaginal administration.

As compared to sublingual route, buccal route of administration shows a lower AUC, a lower peak concentration, and lesser side effects. The pattern of absorption by buccal route is also similar to the vaginal route but it produces lower serum levels overall. Nevertheless, the buccal and vaginal routes of administration have similar effects on uterine tone and activity. The buccal route of is also the least variable in drug exposure and peak levels. The efficacy of misoprostol is not altered by the administration of



NSAIDs for pain relief. There are no known drug interactions with misoprostol (16).



**Figure 4:** Mean plasma concentrations of misoprostol acid over time (arrow bars = 1 SD).

(20)

### Side effects

The side effects of misoprostol observed from various studies include maternal pyrexia, shivering, nausea, vomiting, loose stools and abdominal pain. These side effects are dose dependent and therefore, it is better to choose the lowest dose of misoprostol that is most effective which will thereby cause less side effects. Despite the fact that the optimal dose for termination of pregnancy in the second trimester has not been established, administration of 400 mcg vaginally every 6 hours for a 48-hour period may be a reasonable approach.

Usage of misoprostol for MTP in the setting of a previous cesarean section scar,

may be safely performed in the second trimester though it is a contraindication in the third trimester. However, there is not adequate data on the absolute risk of induction of labor in this setting as many studies on second-trimester MTP with misoprostol have excluded patients with a previous cesarean delivery due to the fear of risk of uterine rupture.

Nonetheless, some randomized studies did include patients with a previous cesarean delivery and no adverse effects were noted in these patients. In addition to this, several retrospective studies have specifically addressed this issue on the use of misoprostol for MTPs in second trimester on a scarred uterus. In a large retrospective study on women with a previous cesarean delivery who underwent MTP between 17 and 24 weeks of gestation, 400 mcg of misoprostol was administered orally along with 400 mcg vaginally as the first dose followed by 400 mcg vaginally every 6 hours for a maximum of 5 doses. The main outcomes included hemorrhage requiring transfusion, retained placenta, post-abortal infection, and rupture uterus. They concluded that a previous cesarean delivery did not have any effect on the incidence of complications. Similar results were found in another study of 80 women with 1 or more cesarean section scars who underwent MTP between 13 and 26 weeks of gestation for various indications. For women up to 20 weeks of gestation Misoprostol 400 mcg, was given and for women greater than 20 weeks of gestation, 200 mcg was given vaginally or sublingually, every 6 hours up to 24 hours. The mean IAI was 16.4 hours and it was statistically different in women with and without a scarred uterus due to previous caesarean section. Uterine rupture or scar dehiscence was not reported. The rates of incomplete abortion, blood loss, or sepsis were

also not found to be statistically different.

### Various studies on Misoprostol regimens

**Table 2: Misoprostol-only regimens**

Study name, place and year	Period of gestation	Number of patients	Group 1	Group 2
Koh et al in Singapore in 2017	13 to 23 weeks	77	PGE1 200 mcg PV Q4H x 5 doses maximum	PGE1 400 mcg PV Q4H x 5 doses maximum
Bhattacharjee et al in India in 2012	13 to 20 weeks	295	PGE1 400 mcg PV moistened with 5% acetic acid Q4H x 5 doses (maximum)	PGE1 400 mcg PV dry Q4H x 5 doses (maximum)
Pongsatha et al in Thailand in 2011	14 to 28 weeks	179	PGE1 400 mcg PV moistened with saline Q3H	PGE1 400 mcg PV moistened with acetic acid Q3H
Chaudhuri et al in India in 2010	12 to 20 weeks	185	PGE1 400 mcg PV Q6H x 4 doses maximum	PGE1 400 mcg PV Q12H x 4 doses
Ozerkan et al in Turkey in 2009	13–24	60	PGE1 400 mcg PV loading dose → 200 mcg PGE1 PV Q2H x 5 doses maximum	PGE1 600 mcg PV loading dose → PGE1 400 mcg PV Q4H x 2 doses maximum
Carbonell et al in Cuba in 2008	12 to 20 weeks	210	PGE1 600 mcg PV every Q6H x 4 doses maximum	PGE1 400 mcg PV Q4H x 5 doses maximum
Herabutya et al in Thailand in 2005	14 to 26 weeks	279	PGE1 600 mcg PV Q6H	PGE1 600 mcg PV Q12 H
Dickinson et al in	14 to 26 weeks	56	PGE1 600 mcg PV loading dose 6 h → PGE1	PGE1 400 mcg oral Q3H

Australia in 2003			200 mcg oral Q3H	
Wong et al in China Hong Kong in 2000	14 to 20 weeks	148	PGE1 400 mcg PV Q3H x 5 doses maximum	PGE1 400 mcg PV Q6H x 3 doses maximum

**Table 3: Misoprostol-only routes**

Name, place and year of study	Gestational age (weeks)	Number of patients	Group 1	Group 2
Desai et al in India in 2016	Midtrimester	22	PGE1 600 mcg PV	PGE1 200 mcg intracervical+200 mcg PV
Al et al in Turkey in 2015	13 to 24 weeks	130	PGE1 400 mcg Q3H x 6 doses maximum	PGE1 400 mcg buccal Q3H x 6 doses maximum
Modak et al in India in 2014	13 to 20 weeks	134	PGE1 400 mcg S/L Q3H 5 doses maximum	PGE1 400 mcg PV Q3H x 5 doses maximum
Nautiya et al in India in 2014	12 to 20 weeks	150	PGE1 400 mcg S/L Q4H x 4 doses maximum	PGE1 400 mcg PV Q4H x 4 doses maximum (3rd group) 400 mcg Q4H x 4 doses maximum
Ellis et al in USA in 2010	17 to 23 weeks	64	PGE1 400 mcg buccal loading dose → PGE1 200 mcg buccal Q5–6H	PGE1 400 mcg vaginal loading dose → PGE1 200 mcg PV Q5–6H
Von Hertzen et al in India, Vietnam, Hungary, Georgia,	13 to 20 weeks	681	PGE1 400 mcg S/L + placebo PV	PGE1 400 mcg PV + placebo

South Africa, Armenia, Slovenia in 2009			Q3H x 5 doses maximum	S/L Q3H x 5 doses maximum
Bhattacharjee et al in India in 2008	13 to 20 weeks	277	PGE1 400 mcg S/L Q3H x 5 doses	PG1 400 mcg PV Q3H x 5 doses maximum
Tang et al in Hong Kong, China in 2004	12 to 20 weeks	220	PGE1 400 mcg S/L Q3H x 5 doses maximum	PGE1 400 mcg PV Q3H x 5 doses maximum
Akoury et al in Canada in 2004	15 to 24 weeks	136	PGE1 400 mcg PV Q4H x 6 doses maximum	PGE1 400 mcg PO Q4 h x 6 doses maximum
Dickinson et al in Australia in 2003	14 to 26 weeks	57	PGE1 400 mcg PV Q6 H	PGE1 400 mcg PO Q3H
Gilbert et al in New Zealand in 2001	Midtrimester	54	PGE1 400 mcg PV loading dose 2 h → 200 mcg PV Q4H	PGE1 400 mcg PV loading dose 2 h → 200 mcg PV PO Q4H

### Misoprostol in second trimester MTPs

Misoprostol is an effective drug for termination of pregnancy in the second trimester. The optimal dose, route of administration and schedule are yet to be determined though there are several randomized, controlled trials examining the different doses and schedules. In these randomized control trials doses ranged from 200 mcg to 800 mcg for vaginal administration and the interval between dosing ranged from every 3 hours to every

12 hours. However, there is no clear-cut conclusive evidence of superiority of one dose or schedule over another drawn from these studies.

In 2003, Dickinson and Evans performed an important study to answer the question of dose optimization. Misoprostol was administered vaginally as 200 mcg every 6 hours, 400 mcg every 6 hours, or a 600-mcg loading dose followed by 200 mcg every 6 hours. Both the 400 mcg and 600/200 mcg regimens were superior to the 200-mcg regimen in terms of median time to expulsion. The side effects were more with 600/200 mcg regimen than the other 2 dosing schedules. (21)

FIGO recommends 400 mcg per vaginum (PV) for every three hours for termination of pregnancy between 13 and 24 weeks of gestation. For fetal death between 13 and 26 weeks, FIGO recommends 200 mcg per vaginal / sublingual / buccal for every 4 to 6 hours

## **MIFEPRISTONE**

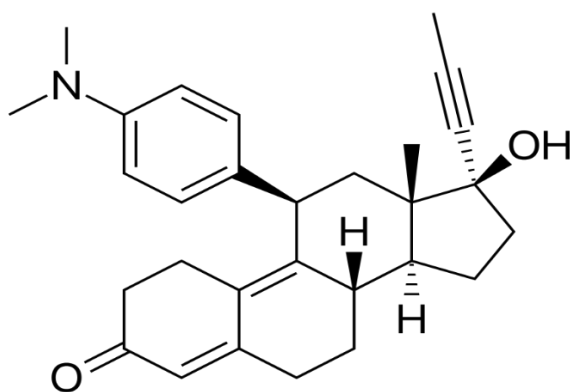
Mifepristone commonly known as RU-486 was invented in France by Dr Etienne - Emile Beaulieu in 1980. It was named after the pharmaceutical company Roussel Uclaf and an arbitrary lab serial number. It was invented when they were investigating compounds that would block glucocorticoid receptors. It was noticed that some of the compounds bound strongly to the similarly shaped progesterone receptor and blocked the action of progesterone.

In 1982 when “Effect of an antiprogestone in women, interruption of menstrual cycle and of early pregnancy” was presented before French Academic des Sciences, the potential of RU486 as an abortifacient was noted.

Mifepristone is a steroidal antiprogestogen, an anti-glucocorticoid and anti-androgen to a much lesser degree. Mifepristone is competitive progesterone receptor antagonist when progesterone is absent. But when progesterone is present, mifepristone acts as a partial agonist. It is a 19-nor steroid which has a hydrophobic 1 propyl substituent at  $17\alpha$  position which increases its progesterone receptor binding affinity. Because of its weak progestational effect on the decidua when progesterone is absent, either during anovulatory cycles or after menopause, it is considered to be a progesterone receptor modulator, Mifepristone is derived from the synthetic progestin norethindrone.

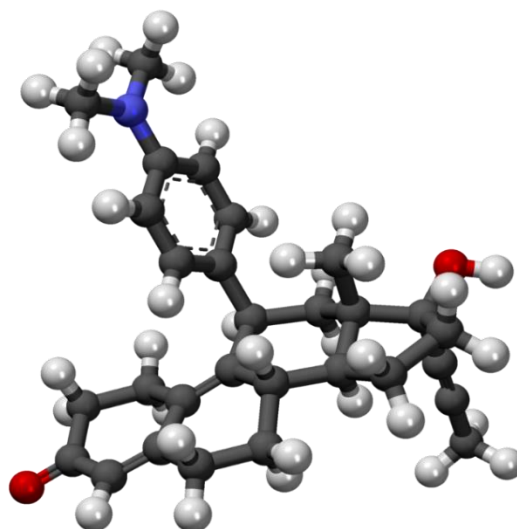
**Figure 5:**

Chemical structure of Mifepristone(22)



**Figure 6:**

Molecular structure of Mifepristone (23)



**Figure 7:** Mifepristone + Misoprostol tablets(24)





During the first 3 days of the follicular phase of menstrual cycle, administration of this drug has no effect. Whereas in the late luteal phase it causes luteolysis and prevents pregnancy.

The action of Mifepristone in medical abortions is as follows:

- causes decidual degeneration by blocking the progesterone receptors on the endometrium
- releases endogenous prostaglandins
- also increases the sensitivity of myometrium to the contractile effects of exogenous prostaglandins and it shortens induction- abortion interval and reduction in doses of prostaglandins required.
- causes cervical ripening and dilatation

Mifepristone administration in the early stages of pregnancy causes decidual breakdown by blockade of uterine progesterone receptors. Mifepristone, being a progesterone receptor antagonist causes breakdown of maternal capillaries in the decidua. The breakdown of decidua leads to detachment of the blastocyte, which in turn decreases hCG production. This causes a decrease in progesterone secretion from the corpus luteum, which further contributes to decidual breakdown. Decreased endogenous progesterone along with progesterone receptors blockade in the uterus causes increase in synthesis of prostaglandins by the epithelium of decidua glandular cells and thereby sensitizes the myometrium to the contractile actions of prostaglandins. All these effects appear within

24-48 hour of their use.

When Mifepristone is administered 24-48 hours prior to prostaglandins, the sensitivity to prostaglandins is about 5-fold increased. When a single oral dose of 100 mg is given, the concentration of Mifepristone in fetal cord blood ranges from 200 ng/ml (30 minutes) to 400ng/ml (18hrs).

The peak maternal concentration in 12 hours is 1500 ng/ml and fetal- maternal ratio is 0.33. Mifepristone 200 mg is found to be more effective than 600 mg when given prior to prostaglandins in inducing medical abortions.

#### PHARMOKINETICS: -

The bioavailability of Mifepristone is 60% and the half- life is 26 to 30 hours. It is mainly metabolized in the liver and the enzyme CYP3A4 plays an important role in its metabolism. Its excretion is through bile and then through faeces. By binding to alpha acid glycoprotein, Mifepristone gets saturated very fast. It has been noted that it interacts with drugs like erythromycin and Ketoconazole which are CYP 3A4 inhibitors. But with drugs like Rifampicin and anticonvulsants, about 85% of Mifepristone is absorbed.

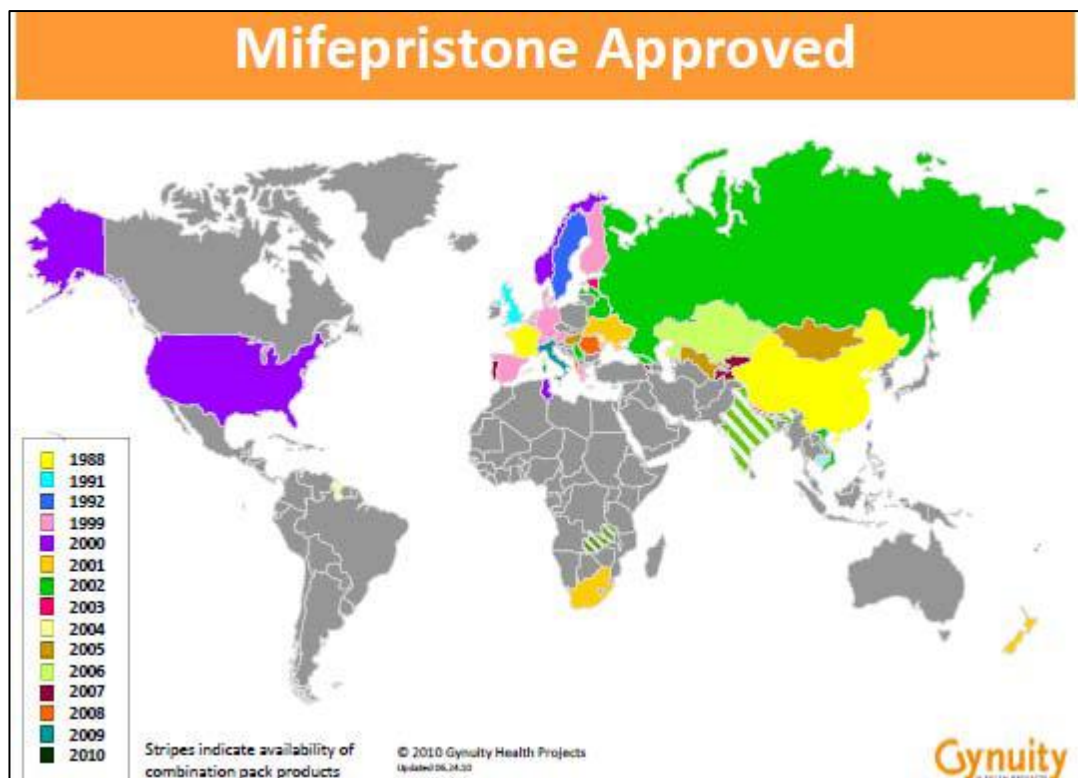
Side effects: Though side effects with Mifepristone is rare, the most common side effects are headache, gastrointestinal symptoms like nausea, vomiting, and diarrhea. The other side effects are skin rash, giddiness and long-term use can result in endometrial hyperplasia by reducing the effect of progesterone on the endometrium. It also causes hypokalemia and rise in creatinine levels.

Contraindications: - Hypertension, cardiovascular diseases, asthma, anemia, glaucoma, adrenal failure, hemorrhagic disorders, woman on anticoagulant, inherited porphyria, glucocorticoid therapy, smoking. Scarred uterus, lactating woman, presence of IUCD, ectopic pregnancy,

Less common: - cough, common cold, breathing difficulty, wheezing, tightness of chest, headache, heartburn.

Other uses: - Leiomyoma uterus, endometriosis, ca ovary, ca breast, glaucoma, Cushing's syndrome, meningiomas, ca prostate and as emergency contraceptive.

**Figure 8:** Countries where Mifepristone is available (25)



## Various studies on Mifepristone- Misoprostol combination

**Table 4: Mifepristone- Misoprostol dosing regimen**

Author	Period of gestation	Number of patients	Group 1	Group 2
Naravage et al in Thailand, India, Vietnam, Sweden in 2017	9 to 20 weeks	100	200 mg MF PO 24 h→ 800 mcg PGE1 PV loading dose→ 400 mcg PGE1 S/L Q3H x 4 doses maximum	200 mg MF PO 48 h→ 800 mcg PGE1 PV loading dose→ 400 mcg PGE1 S/L Q3H x 4 doses maximum
Abbas et al in Vietnam in 2016	12 to 22 weeks	509	200 mg MF PO + 400 mcg PGE1 buccal (given together) → 400 mcg PG1 buccal Q3H	200 mg MF oral 24 h→ 400 mcg PGE1 buccal Q3H
Chaudhuri et al in India in 2014	13 to 20 weeks	95	200 mg MF PO 24 h→ 800 mcg PGE1 PV loading dose → 400 mcg PG1 PV Q3H x 4 doses maximum	200 mg MF PO 48 h→ 800 mcg PGE1 PV loading dose → 400 mcg PGE1 PV Q3H x 4 doses maximum
Chen et al in China in 2013	8 to 16 weeks	1112	200 mg MF PO 24 h→ 600 mcg PGE1 PV loading dose→ 600 mcg PG1 PO Q3H x 4 doses maximum	200 mg mifepristone PO 24 h→ 600 mcg PGE1 PO Q3H x 4 doses maximum
			(3rd group) 100 mg MF PO 24 & 48 h→	(4th group) 200 mg MF PO 24 h→

			600 mcg PGE1 PV Q12H x 3 doses maximum	600 mcg PGE1 PV Q3H x 4 doses maximum
Jinfeng et al in China in 2013	8 to 16 weeks	327	100 mg MF PO 24 & 48 h→ 400 mcg PGE1 oral Q3H x 4 doses	24 & 48 h→ 600 mcg PV PGE1 loading dose → 400 mcg PGE1 PV Q6H, x 4 doses maximum
Mentula et al in Finland in 2011	13 to 24 weeks	227	200 mg MF PO 24 h→ 400 mcg PGE1 PV Q3H x 5 doses maximum	200 mg MF PO 48 h→ 400 mcg PGE1 PV Q3H x 5 doses maximum
Hou et al in China in 2010	13 to 16 weeks	100	200 mg MF PO 24 h→ 600 mcg PGE1 PV loading dose → 400 mcg PGE1 PO Q6H x 2 doses maximum	200 mg MF PO 48 h→ 600 mcg PGE1 PV loading dose → 400 mcg PGE1 PO Q6H x 2 doses
Chai et al in China, Hong Kong, China in 2009	12 to 20 weeks	141	200 mg MF PO + 600 mcg PGE1 PV loading dose (given together) → 400 mcg PGE1 PV Q3H x 4 doses maximum	200 mg MF PO 36–38 h→ 600 mcg PGE1 PV loading dose→ 400 mcg PGE1 PV Q3H x 4 doses maximum
Webster in UK in 1996	13 to 20 weeks	70	600 mg MF PO 36–48 h→ 800 mcg PGE1 PV loading dose → 400 mcg PGE1 PO Q3H x 4 doses maximum	200 mg MF PO 36–48 h→ 800 mcg PGE1 loading dose → 400 mcg PGE1 PO Q3H x 4 doses maximum

**Table 5: Mifepristone- Misoprostol dosing routes**

Name, Place and year of study	Period of gestation	Number of patients	Group 1	Group 2
Dabash et al in Uzbekistan, Tunisia, Nepal, Armenia	13 to 21 weeks	339	200 mg MF PO 24 h→ 400 mcg PGE1 buccal Q3H	200 mg MF PO 24 h→ 400 mcg PGE1 S/L Q3H
Garg et al in India in 2015	14 to 25 weeks	50	200 mg MF PO 48 h→ 400 mcg PGE1 buccal loading dose → 200 mcg PGE1 buccal Q6H x 6 doses maximum	200 mg MF PO 48 h→ 200 mcg PGE1 PV Q6H x 6 doses maximum
Dickinson et al in Australia in 2014	14 to 22 weeks	302	200 mg MF PO 24 to 48 h→ 800 mcg PGE1 PV loading dose → 400 mcg PGE1 PV Q4H x 5 doses maximum	200 mg MF PO 24–48 h→ 800 mcg PGE1 PV loading dose → 400 mcg PGE1 S/L Q4H x 5 doses maximum (3rd group) 200 mg MF PO 24–48 h→ 800 mcg PGE1 PV loading dose → 400 mcg PGE1 PO Q4H x 5 doses maximum
Chen et al in China in 2013	8 to 16 weeks	556	200 mg MF PO 24 h→ 600 mcg PGE1 PO Q3H x 4 doses maximum	200 mg MF PO 24 h→ 600 mcg PGE1 PV Q3H x 4 doses maximum

Hamoda et al in UK in 2005	13 to 20 weeks	76	200 mg MF PO 36–48 h→ 600 mcg PGE1 S/L loading dose → 400 mcg PGE1 S/L Q3H x 5 doses maximum	200 mg MF PO 36–48 h→ 800 mcg PGE1 PV loading dose → 400 mcg PGE1 PV Q3H x 5 doses maximum
Tang et al in China, Hong Kong in 2005	12 to 20 weeks	118	200 mg MF PO 36–48 h→ 400 mcg PGE1 PO + placebo S/L Q3H x 5 doses	36–48 h→ 400 mcg PGE1 S/L + placebo PO Q3H x 5 doses
Ngai et al in China, Hong Kong in 2000	14 to 20 weeks	139	200 mg MF PO 36–48 h→ 400 mcg PGE1 PO + placebo PV Q3H x 5 doses maximum	200 mg MF PO 36–48 h→ 200 mcg PGE1 PV+ placebo PO Q3H x 5 doses maximum
Ho et al in China, Hong Kong in 1997	14 to 20 weeks	98	200 mg MF PO 36–48 h→ 400 mcg PGE1 PO + placebo PV Q3H x 5 doses maximum	200 mg MF PO 36–48 h→ 200 mcg PGE1 PV + placebo PO Q3H x 5 doses maximum
El-Refaey et al in UK in 1995	13 to 20 weeks	69	600 mg MF PO 36–48 h→ 600 mcg PGE1 PV loading dose → 400 mcg PGE1 PV Q3H	600 mg MF PO 36–48 h→ 600 mcg PGE1 PV loading dose → 400 mcg PGE1 PO Q3H

**Table 6: Mifepristone–misoprostol vs. misoprostol only**

Name, place and year of study	Period of gestation	Number of patients	Group 1	Group 2
Akkenapally et al in India in 2016	14 to 20 weeks	200	200 mg MF PO 24 h→ 600 mcg PGE1 PV loading dose→ 400 mcg PGE1 S/L Q3H x 5 doses maximum	600 mcg PGE1 PV loading dose→ 400 mcg PGE1 S/L Q3H x 5 doses maximum
Dabash et al in Tunisia in 2015	14 to 21 weeks	120	200 mg MF PO 24 h→ 400 mcg PGE1 buccal Q3H x 5 doses maximum	Placebo 24 h→ 400 mcg PGE1 buccal Q3H x 5 doses maximum
Kulkarni et al in India in 2014	13 to 20 weeks	60	200 mg MF PO 48 h→ 400 mcg PGE1 PV loading dose→ 200 mcg PGE1 PV Q6H	Placebo 48 h→ 400 mcg PGE1 PV loading dose→ 200 mcg PGE1 PV Q6H
Mukhopadhyay et al in India in 2012	12 to 20 weeks	122	200 mg MF PO 48 h→	Placebo 48 h→



			400 mcg PGE1 PV loading dose→ 200 mcg PGE1 PV Q4H x 5 doses maximum	400 mcg PGE1 PV loading dose→ 200 mcg PGE1 PV Q4H x 5 doses maximum
Nagaria et al in India in 2011	12 to 28 weeks	200	200 mg MF PO 12 h → 600 mcg PGE1 PV loading dose → 300 mcg PGE1 Q3H x 5 doses maximum	600 mcg PGE1 PV loading dose → 300 mcg PGE1 PV Q3H x 5 doses maximum
Ngoc et al in Vietnam in 2011	14 to 21 weeks	260	200 mg MF PO 24 h→ 400 mcg PGE1 buccal Q3H x 5 doses maximum	24 h→ 400 mcg PGE1 buccal Q3H x 5 doses maximum
Kapp et al in USA in 2007	18 to 23 weeks	64	200 mg MF Po 24 h→ 400 mcg PGE1 buccal loading dose→ 200 mcg PGE1 buccal Q6H	Placebo 24 h→ 400 mcg PGE1 buccal loading dose→ 200 mcg PGE1 buccal Q6H

D.R. Urquhant and A.A. Templeton conducted a study by giving Mifepristone 600 mg 24, 36 & 48 hours prior to prostaglandin extra-amniotic infusion. In this group, bleeding was not observed in any of the groups prior to prostaglandins infusion. This study

reported that Mifepristone can be safely given prior to admission to the hospital for termination (26).

Similarly, a prospective open-label study conducted by Ingrida Platais et al. aimed to assess the feasibility and acceptability of a second-trimester medical abortion regimen using Mifepristone and sublingual Misoprostol, concluded that medical abortion in pregnancies of 13–22 weeks with 200 mg Mifepristone followed 24–48 hours later by 400 mcg sublingual Misoprostol administered every 3 hours until complete expulsion, is effective, safe and acceptable to women. Women can be given the option to take Mifepristone at home and return to the hospital (27).

Furthermore, Natalia Prodan et al conducted a retrospective study to compare Mifepristone & Misoprostol strategies in second trimester termination of pregnancies and to determine which is more effective in accelerating time to delivery. This study suggested that if Mifepristone is administered 1 day prior to induction, delivery occurs in more than 90% of the cases within 24 h after the first induction (28).

Ngoc NT, Shochet T, Raghavan S, et al. conducted a randomized, placebo-controlled, double-blind trial in Vietnam, to estimate the clinical benefit of pretreatment with Mifepristone followed by Misoprostol compared with Misoprostol alone for second-trimester abortion. The study concluded that Mifepristone when given in combination with Misoprostol, the chances of complete abortion was more than twice than in 15 hours. The mean IAI for complete abortion was shorter among participants who were given Mifepristone prior to Misoprostol compared with that given misoprostol alone and the

difference was statistically significant. The side effect profiles for the two regimens did not differ significantly and acceptability of the treatments was high (29).

A randomized double-blind placebo-controlled trial by Dabash et al to assess the difference in outcome of Misoprostol with or without Mifepristone in second trimester abortions concluded that adding Mifepristone before Misoprostol can improve the quality of second trimester abortion care by making the process faster (30).

A prospective study was carried out by Maninder Kaur et al to find out the safety and effectiveness of pretreatment with Mifepristone prior to Misoprostol for mid trimester MTP. Data was analyzed for 48 cases who fulfilled the inclusion criteria. Complete abortion occurred in 36 (75%) of cases, 13(25%) required dilatation & curettage for incomplete abortion including manual removal of placenta in 8 cases. Seven patients with a previous uterine scar due to caesarean section had complete abortion. Seven women in the study were with history of previous caesarean section and all of them had complete evacuation. The study concluded that pretreatment with Mifepristone before Misoprostol administration is an effective & safe method for MTP in second trimester. It can be effectively used in patients with previous caesarean scar with close supervision (31).

Kulkarni Kranti K. conducted a prospective study to assess the efficacy and safety of combining Mifepristone before Misoprostol use in second trimester to considerably reduce the induction– abortion interval with the lowest possible dose and adverse reaction. This study, like many others, offers a reliable, safe, and cost-effective option by combining Mifepristone before Misoprostol to decrease the induction– abortion interval (32).

ACOG guidelines for second trimester MTP (2013) - 200mg of Mifepristone, administered orally, and 24-48 hours later 800mcg of misoprostol administered vaginally and then 400 mcg of misoprostol administered vaginally or sublingually 3-hourly up to maximum 5 doses (33).

RCOG best practice in second trimester MTP (2015) - Mifepristone 200 mg orally, followed by 36- 48 hours later by Misoprostol 800 mcg vaginally, then Misoprostol 400 mcg per oral or per vaginum, every 3 hours, to a maximum of four further doses. If abortion does not occur, Mifepristone can be repeated 3 hours after the last dose of Misoprostol and 12 hours later misoprostol may be recommended. (34).

WHO recommendation for second trimester MTP - Oral Mifepristone followed 36 to 48 hours by Misoprostol followed by Misoprostol 800 mcg vaginally or 400 mcg orally. Repeat Misoprostol 400 mcg, either vaginally or sublingually, every 3 hours up to four further doses. Guideline in the region where Mifepristone is not available or not affordable - Misoprostol 400 mcg vaginal or sublingual. Repeat every 3 hours for up to five doses (35).

Medical termination of pregnancy with Misoprostol alone is effective, though higher doses are needed; side effects were more frequent and induction to abortion interval was noted to be longer compared with the combined treatment with Mifepristone plus Misoprostol. Misoprostol alone can be used in places where Mifepristone is unavailable or is not affordable. Misoprostol is cheap and is easily available in India.

The disadvantage of Mifepristone is that it is expensive and it is effective only when combined with Misoprostol. Tablet Mifepristone 200 mg, is usually given 24- 36 hours prior to Misoprostol administration and this regimen has been noted to give a high expulsion rate of 91 to 96% as seen in various studies.

## **MATERIALS AND METHODS**

### **Research design**

This was a prospective observational cohort study.

### **Study setting:**

The study was approved by the Institutional Review Board of Christian Medical College and Hospital, Vellore. It was conducted between January 2021 and October 2021. Patients were recruited from the obstetric wards of the Department of Obstetrics and Gynecology, Christian Medical College Vellore, following an informed consent. A total of 100 women who met the inclusion criteria were recruited for the study.

### **Inclusion criteria**

1. Pregnancies between 12 weeks and 20 weeks of gestation (based on menstrual history and dating ultrasound)
2. Women with a closed cervical os and no vaginal bleeding
3. Women who fulfil the indications defined in the MTP act of India 1971

### **Exclusion criteria**

- Women who are in the process of abortion.
- Women less than 12 weeks or more than 20 weeks gestation.
- Patients with known allergy or contraindication to the use of Mifepristone or Misoprostol

### **Sample size:**

A 3-month audit of all the termination of pregnancies between 12-20 weeks of gestation in our department was done. It was observed that of the 35 terminations, 20 were done by administration of Misoprostol alone and 15 were done by combining Mifepristone and Misoprostol. Based on this pilot data, the induction abortion interval standard deviation in the Misoprostol group was 12.41 hours and in the combination drug group was 8.67 hours respectively. The mean difference between the two groups was 6.78 hours with 5% error and 90% power. Hence the required sample size was total 110 subjects with 55 subjects in each group. Finally, we achieved 55 subjects in Misoprostol group and 45 subjects in the combination drug group.

**Method:**

This was an observational prospective cohort study which was done over a total period of 10 months from January 2021 to October 2021. Women who got admitted in obstetric wards for termination of pregnancy between 12 and 20 weeks, who met the eligibility criteria were recruited for the study. The pregnancies that underwent medical terminations in between 12 and 20 weeks of gestation were classified into 2 groups. The group A who received Tab Misoprostol alone (Dosage according to FIGO recommendations) and Group B who received Tab Mifepristone 200 mg at home followed by in –patient Tab Misoprostol administration after 24-48 hours.

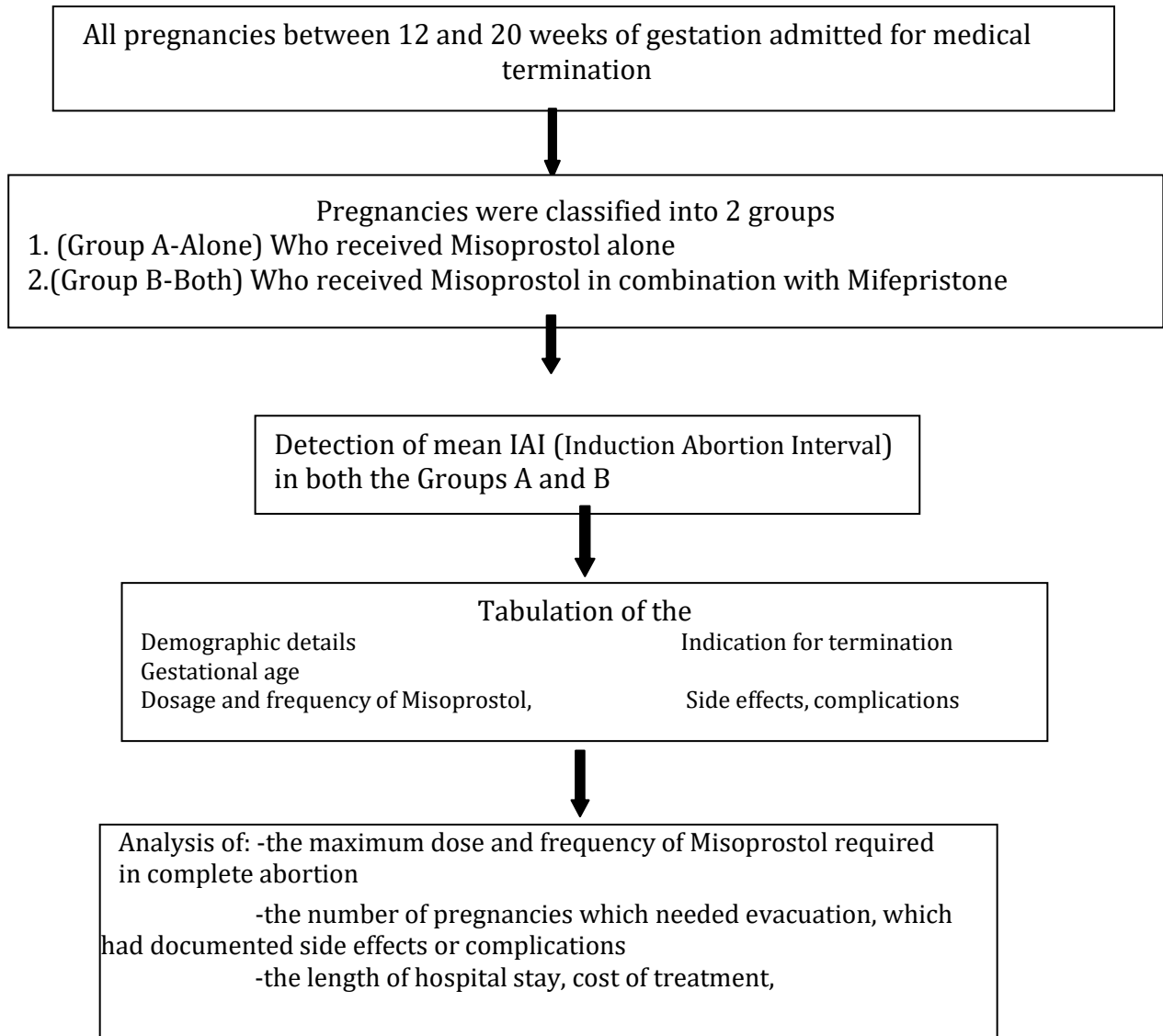
Written informed consent was taken. All available data on the patient’s demographic details, gestational age, indication for termination, dosage and frequency of Misoprostol, IAI, side effects, complications, length of hospital stay and the final bill were collected. The information collected were recorded in detail, filled in proforma and entered in epidata form.

**Statistical Methods:**

Descriptive statistics were used. Data was summarized using Mean (SD) or median (IQR) for continuous variables. Categorical data were expressed as number and percentage. Comparisons between the means for groups was done by using an independent t test for normally distributed data and Mann-Whitney U test for data with non-normal distribution after which the median (IQR) was reported. Generalized linear model was used to compare the effect size between the groups after adjustment with other variables. P value less than 0.05 was considered as statistical significance. All the statistical analysis was performed using SPSS 21.0 version.



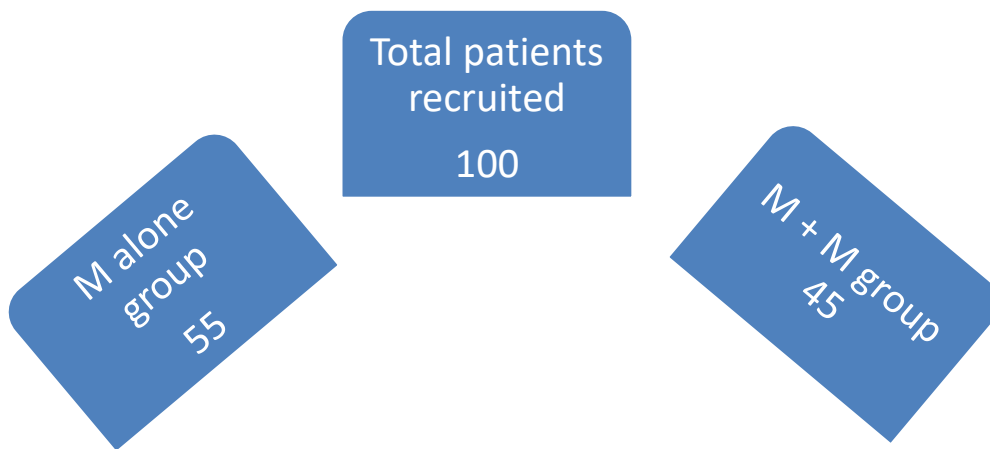
### Detailed diagrammatic Algorithm of the study



## **RESULTS**

Over a period of 10 months from January 2021 to October 2021 a total of 100 cases has been recruited for this study. There were 55 women were in the Misoprostol alone group and 45 women were in combination regimen group {mifepristone + misoprostol}.

**Figure 9: Number of patients in the study**



### **Demographic and baseline characteristics of the study population:**

#### **Age**

Most women in our study were in the age group between 26 and 30 years (38%).

Twenty-seven percentage of women were more than 30 years age.

In the 26 to 30 age group, 24 women received the Misoprostol alone [M] and 14 women received both medicine [M+M]. 43.6 % and 37.8 % women belonged to the 26 -30years age group in M alone and combination group respectively.

More than 30 years age group, 17 were in the combination group and 10 in the Misoprostol alone group. 9 % of the patients were less than 20 years of age of which 4 were in the M alone group and 5 in the combination group.

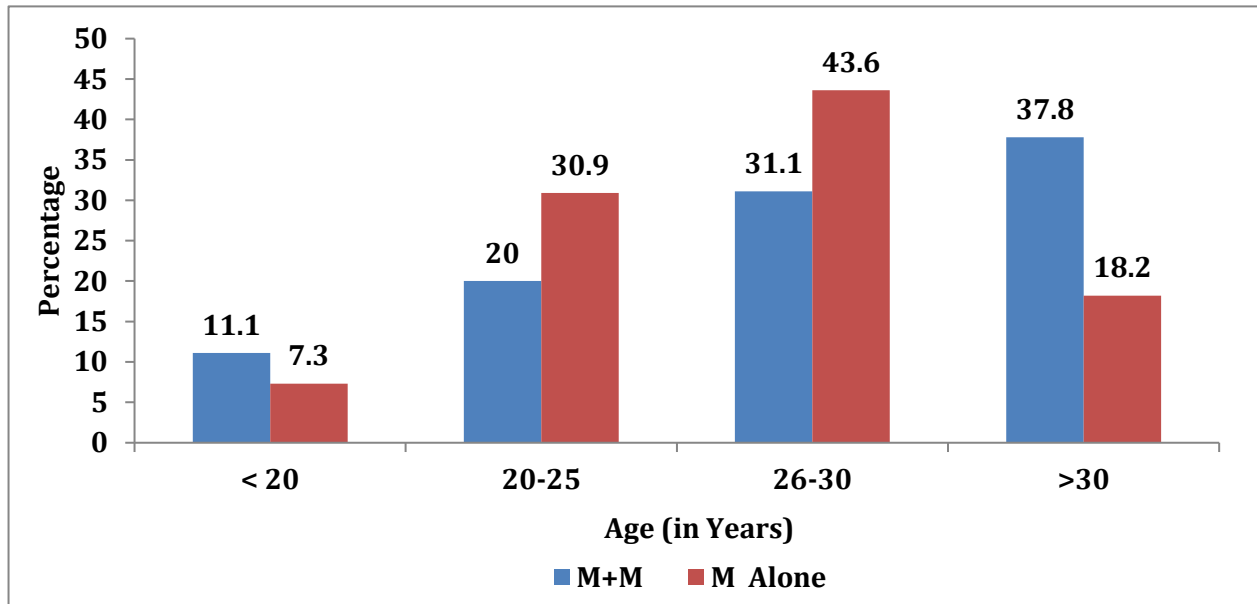
Most number of patients in the combination group were in the more than 30 years group whereas the greatest number of patients in the Misoprostol alone group was in the age group of 26 to 30 years.

The median age in the M alone and combination group was 27.22 years and 28.49 years respectively.

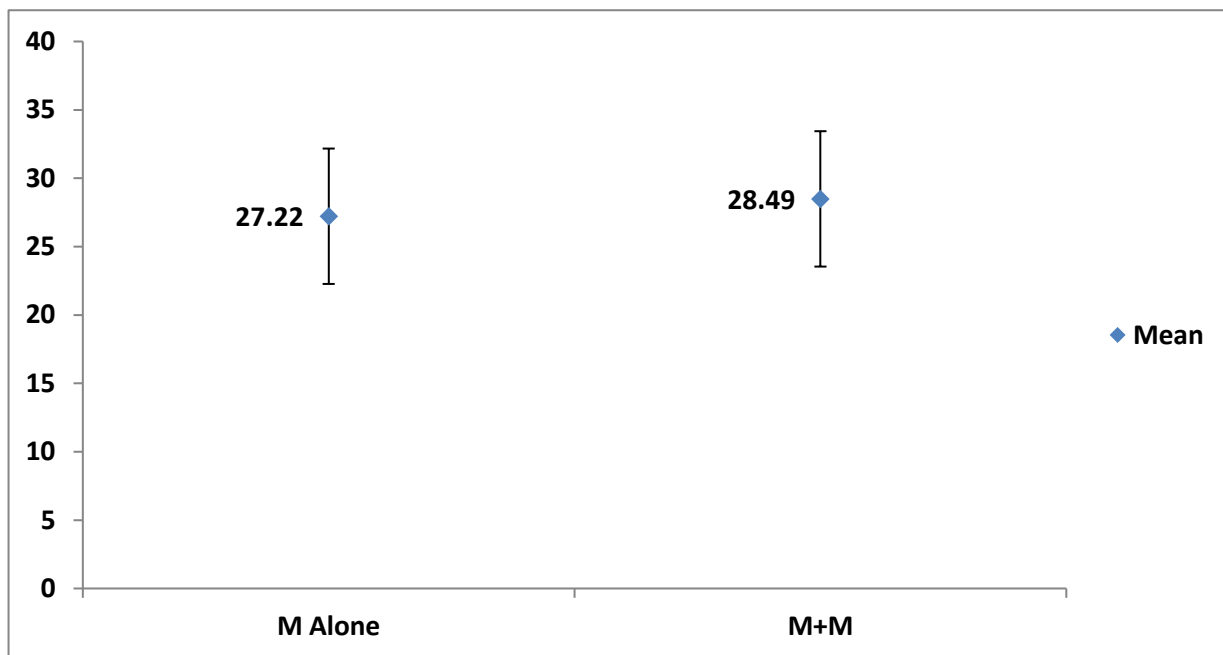
**Table 7: Comparison of age in M and M+ M group**

Groups	M + M		M alone		P – Value
	n	%	n	%	
<b>Age in Years</b>					
< 20	5	11.1	4	7.3	0.108
20-25	9	20.0	17	30.9	
26-30	14	31.1	24	43.6	
>30	17	37.8	10	18.2	

**Figure 10: Bar graph showing comparison of age in M and M+ M group**



**Figure 11: Comparison of Mean age in two groups**



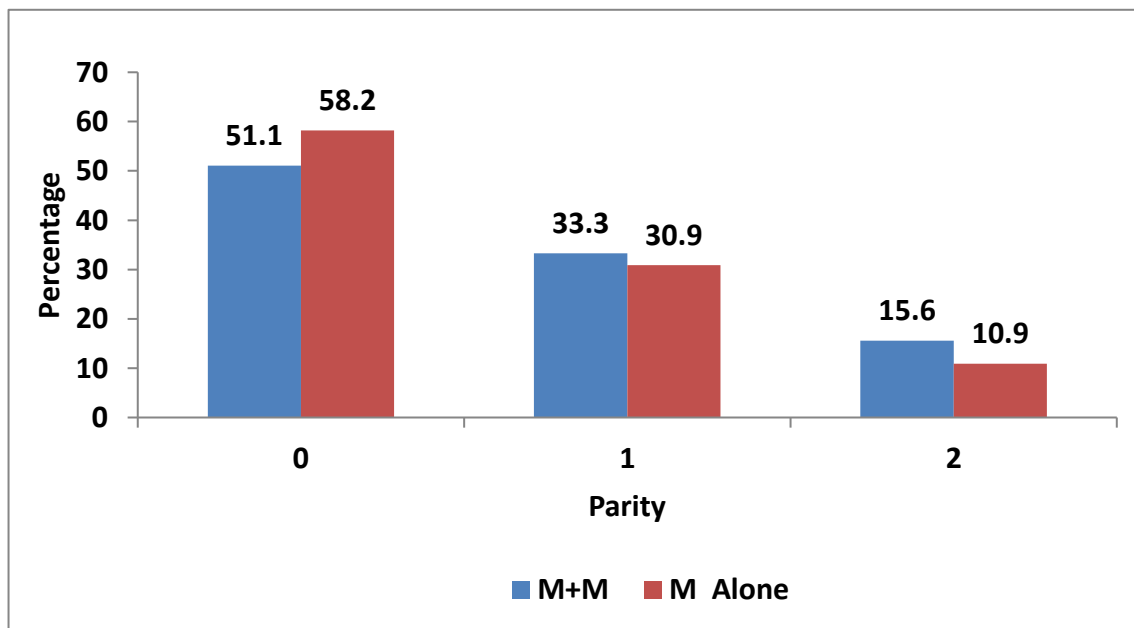
## Parity

Fifty-five percentage of women in the study group were nulliparous of which 32 were in the M alone group and 23 in the combination group. Primigravidae women in the Misoprostol alone group and in the combination group were 58.2 % and 51.1 % respectively.

**Table 8: Distribution of parity between M and M+ M group**

Variables	M + M		M alone		P – Value
	n	%	n	%	
<b>Parity</b>					
0	23	51.1	32	58.2	0.711
1	15	33.3	17	30.9	
2	7	15.6	6	10.9	

**Figure 12: Bar graph showing distribution of parity between M and M+ M group**



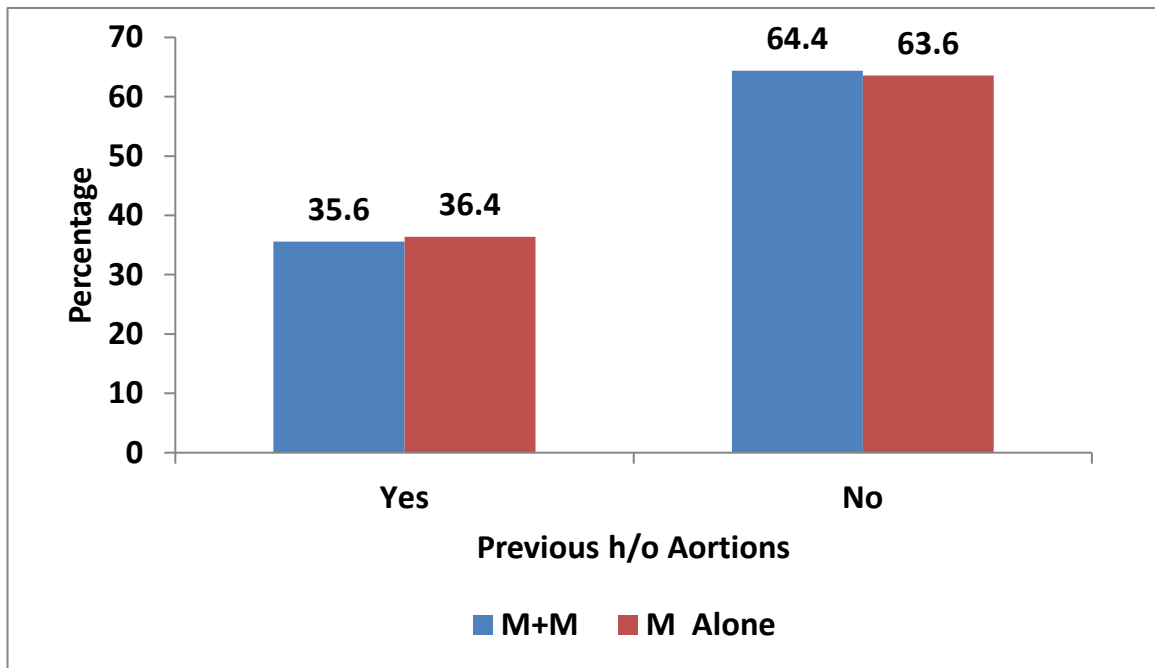
### Previous history of abortions

In our study, 36 percent of the patients had previous history of abortions of which 20 women were in the M alone group and 16 were in the combination group. Women who had history of previous abortion in the M alone group was 36.4 % and 35.6 % patients in the M+M group respectively.

**Table 9: Comparison of previous history of abortions in M and M+ M group**

Groups	M + M		M alone		P – Value
	n	%	n	%	
<b>Previous h/o Abortions</b>					
Yes	16	35.6	20	36.4	0.933
No	29	64.4	35	63.6	

**Figure 13: Bar graph showing comparison of previous history of abortions in M and M+ M group**



### **Gestational age**

In study population gestational age was divided from 12 to 14+6 weeks, 15 to 17+6 weeks and 18 to 20 weeks.

Maximum number of women were in the 12 to 14+6 weeks group. In this group, there were 49 patients of which 25 were in the M alone group and 24 were in the combination group.

Maximum number of women (53.3 %) in the combination group were between 12 to 14.6

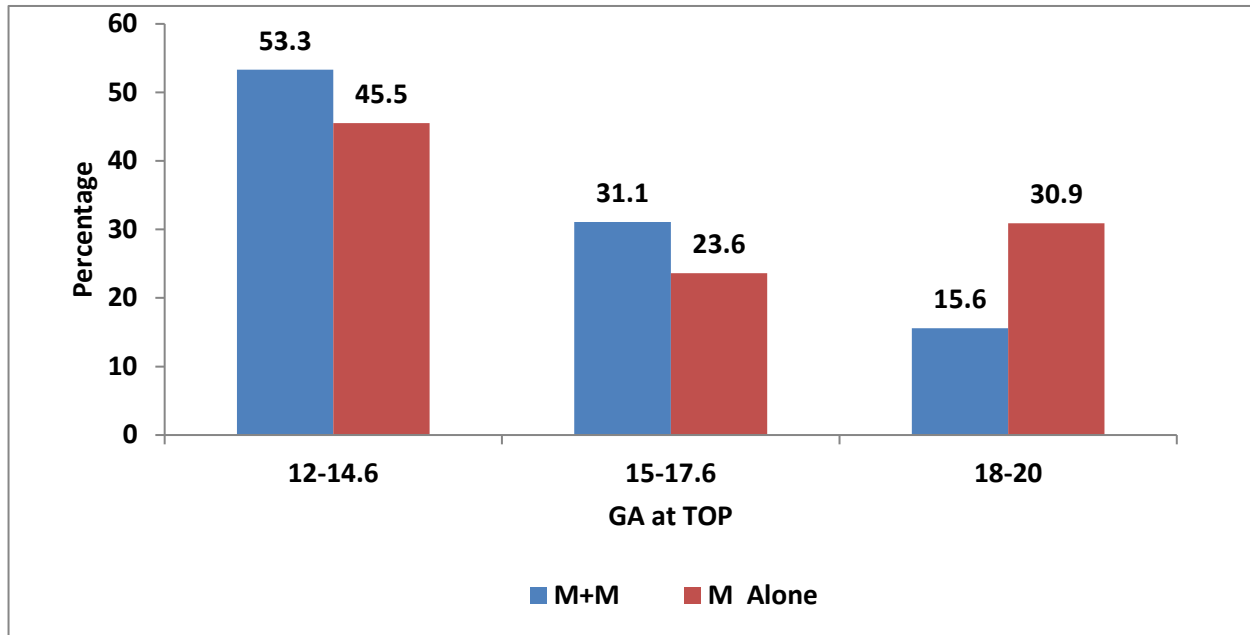
weeks and the least number of patients (15.6%) were between 18-20 weeks. Maximum number of patients (45.5%) in the M alone were also between 12-14.6 weeks and the least number of patients (23.6%) in the M alone group was in the 15-17.6 weeks respectively.

**Table 10: Comparison of gestational age at TOP in M and M+ M group**

<b>Groups</b>	<b>M + M</b>		<b>M alone</b>		<b>P – Value</b>
<b>Variables</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
<b>GA at TOP</b>					
12-14.6	24	53.3	25	45.5	0.196
15-17.6	14	31.1	13	23.6	
18-20	7	15.6	17	30.9	



**Figure 14: Bar graph showing comparison of gestational age at TOP in M and M+M group**



### **Scarred uterus**

Women planned for TOP with previous uterine surgery or previous caesarean section in study group were 11.

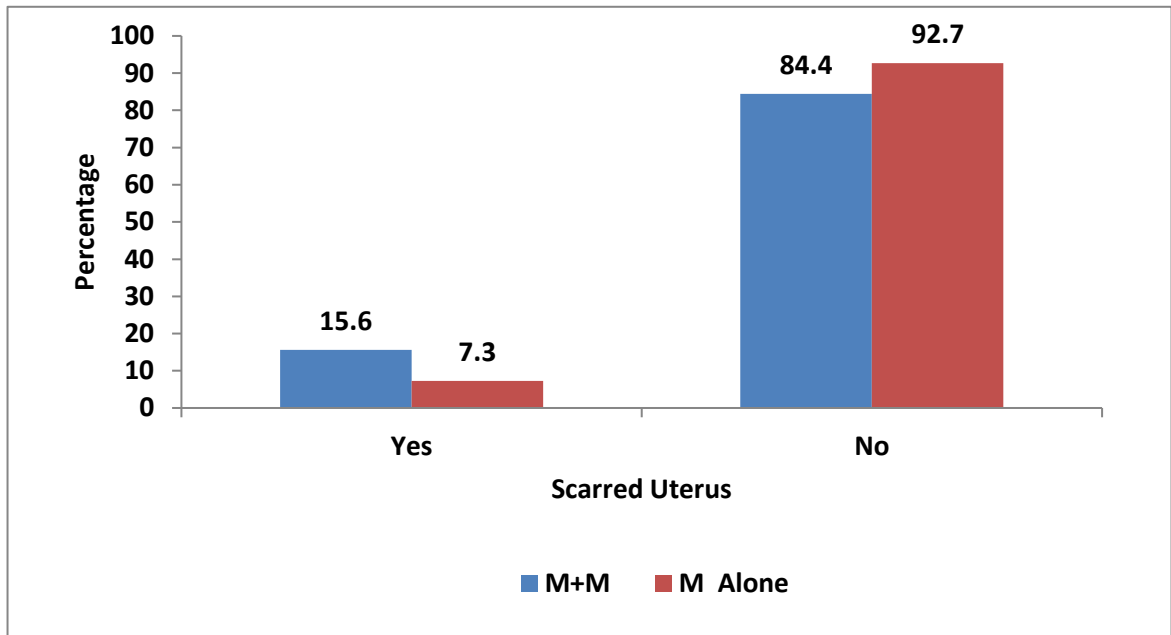
Out of 11, four women received the Misoprostol alone regime and 7 received the combination regime.

7.3 % in the M alone group and 15.6 % in the combination group had a scarred uterus.

**Table 11: Comparison of presence of scarred uterus in M and M+ M group**

Groups	M + M		M alone		P – Value
Variables	n	%	n	%	
<b>Scarred uterus</b>					
Yes	7	15.6	4	7.3	0.214
No	38	84.4	51	92.7	

**Figure 15: Bar graph showing comparison of presence of scarred uterus in M and M+ M group**



## Co-morbidities

**Obstetric co-morbidities** noted in the study group were infertility, scarred uterus, fibroid complicating pregnancy and others.

**Medical co-morbidities** in women planned for TOP were diabetes, hypertension, obesity, thyroid disorders, heart disease, renal disease, autoimmune disorders, seizure disorders and others.

28 percent of the participants in the study had medical co-morbidities and 47 percent had obstetric co-morbidities. 64.4% of women in the combination group had obstetric co-morbidities and 17.8% had medical co-morbidities.

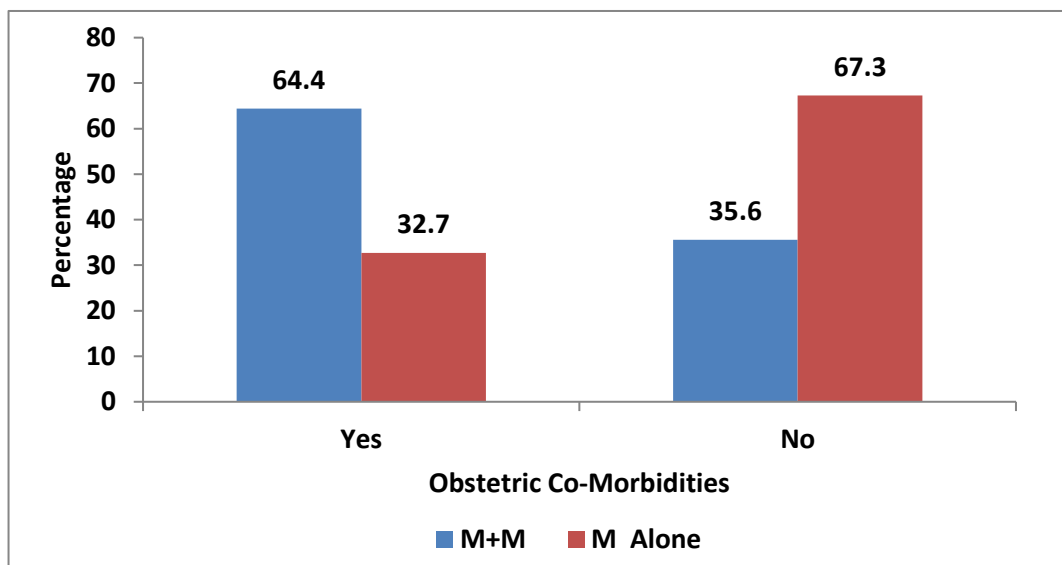
32.7% of participants in the M alone group had obstetric co-morbidities and 36.4% had medical co-morbidities.

**Table 12: Comparison of obstetric co-morbidities in M and M+ M group**

Groups	M + M		M alone		P - Value
	n	%	n	%	
<b>Obstetric Co-morbidities</b>					
Yes	29	64.4	18	32.7	0.002
No	16	35.6	37	67.3	

**Figure 16: Bar graph showing comparison of obstetric co-morbidities in M and M+**

**M group**

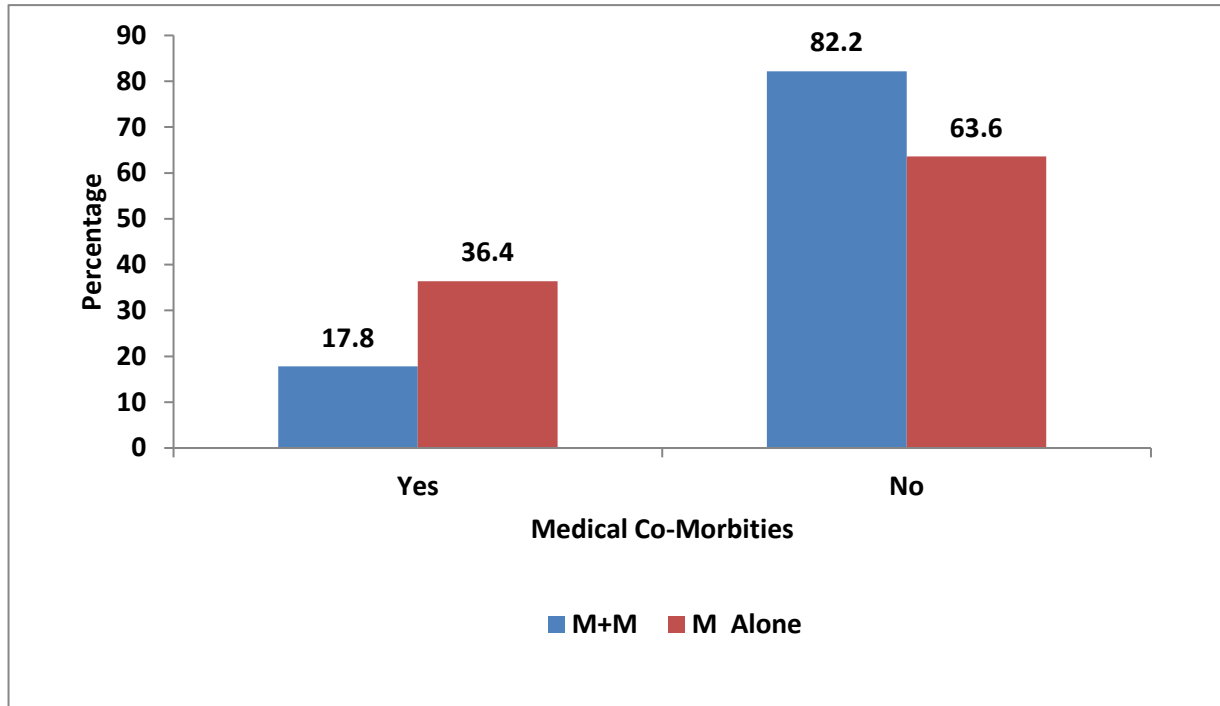


**Table 13: Comparison of medical co-morbidities in M and M+ M group**

Groups	M + M		M alone		P - Value
	n	%	n	%	
<b>Medical Co-morbidities</b>					0.039
Yes	8	17.8	20	36.4	
No	37	82.2	35	63.6	

**Figure 17: Bar graph showing comparison of medical co-morbidities in M and M+**

**M group**



### **Indications of termination**

Of the 100 planned medical terminations of pregnancies, 59 were for fetal indications, 44 were for missed abortion and 3 were for maternal indications.

Of the 59 fetal indications, 16 were due to CNS anomalies, 8 for cardiovascular defects, 3 with lethal renal anomalies, 5 due to lethal skeletal dysplasia and miscellaneous group contained 29 due to syndromes and other fetal indications.

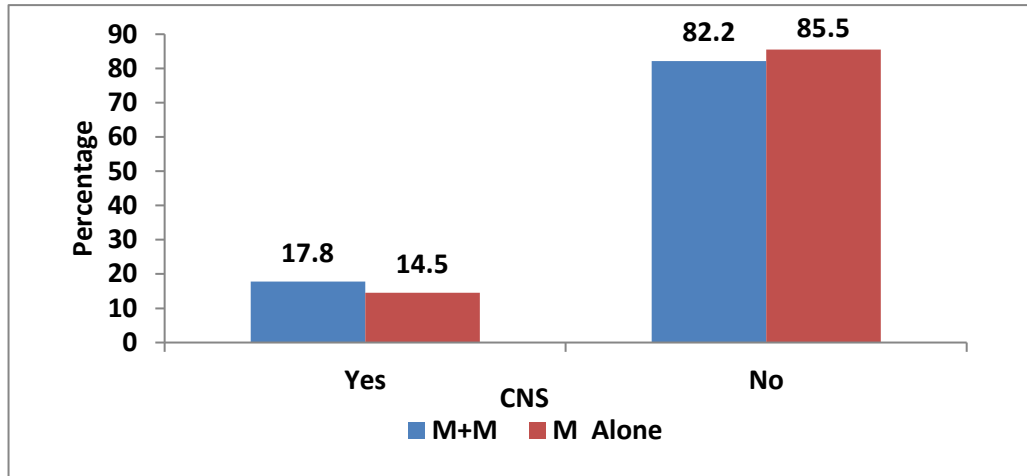
Termination done for maternal indications were rectal carcinoma on chemotherapy, Ebstein anomaly and nephrotic syndrome with uncontrolled hypertension.

**Tables 14 to 18: Comparison of indications for termination according to system wise fetal anomalies in M and M + M group.**

**Table 14: Fetal anomalies (CNS)**

Groups	M + M		M alone		P - Value
	n	%	n	%	
<b>Fetal anomalies:</b>					
<b>CNS</b>					
Yes	8	17.8	8	14.5	0.661
No	37	82.2	47	85.5	

**Figure 18: Bar graph showing comparison of CNS anomalies in M and M + M group.**

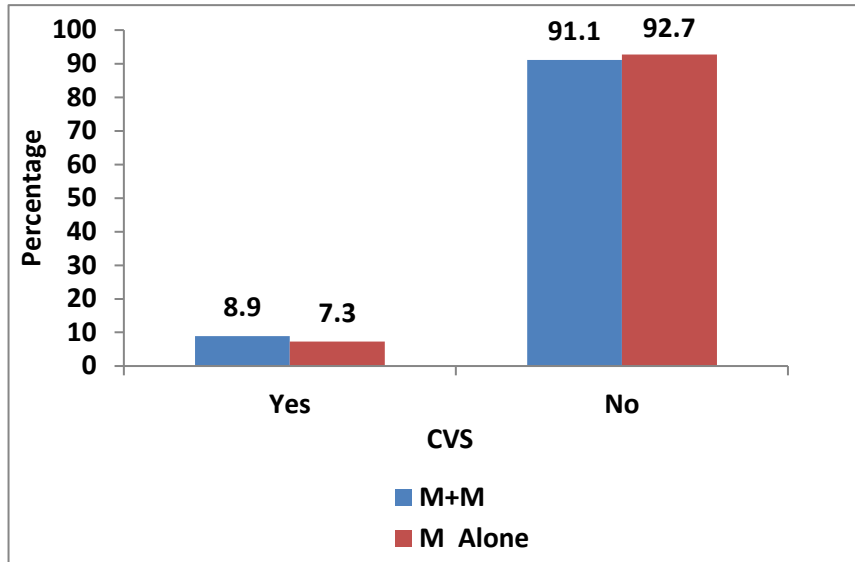


**Fetal anomalies (CVS)**

**Table 15: Fetal anomalies (CVS)**

Groups	M + M		M alone		P – Value
	n	%	n	%	
<b>Fetal anomalies:</b>					
<b>CVS</b>					
Yes	4	8.9	4	7.3	1.000
No	41	91.1	51	92.7	

**Figure 19: Bar graph showing comparison of CVS anomalies in M and M + M group.**



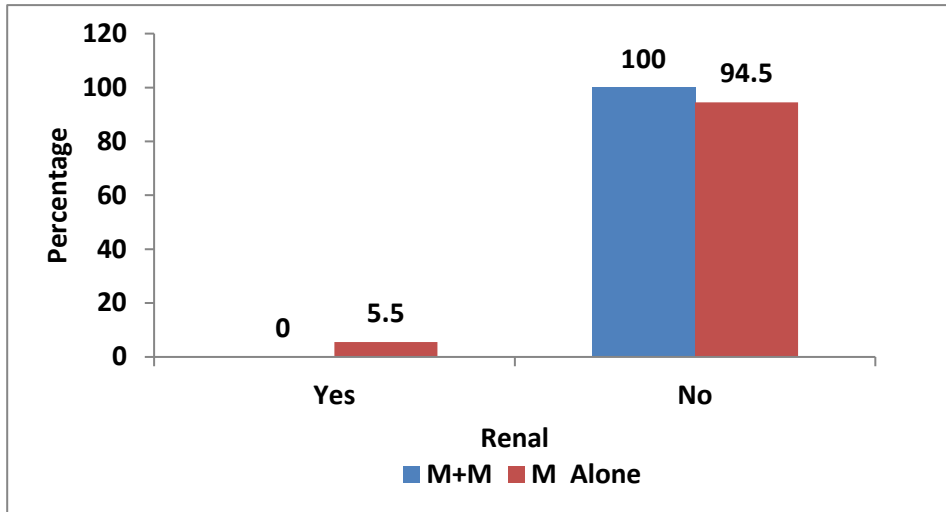
**Fetal anomalies (Renal)**

**Table 16: Fetal anomalies (Renal)**

Groups	M + M		M alone		P - Value
	n	%	n	%	
<b>Fetal anomalies:</b>					
<b>Renal</b>					
Yes	0	0.0	3	5.5	0.250
No	45	100.0	52	94.5	



**Figure 20: Bar graph showing comparison of renal anomalies in M and M + M group.**

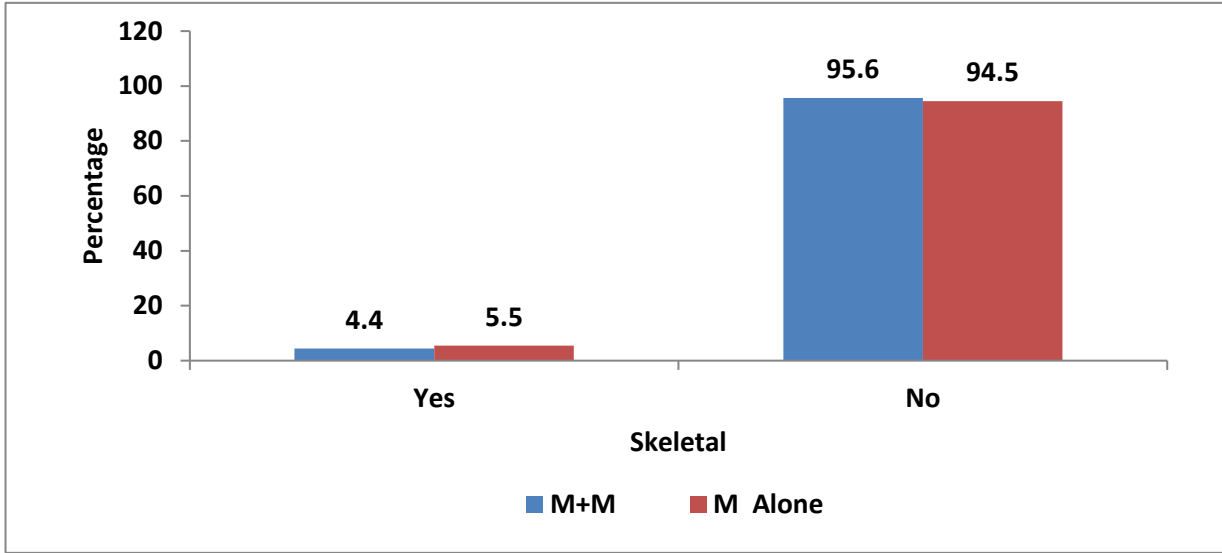


**Fetal anomalies (Skeletal)**

**Table 17: Fetal anomalies (Skeletal)**

Groups	M + M		M alone		P - Value
	n	%	n	%	
<b>Variables</b>					
<b>Fetal anomalies:</b>					
<b>Skeletal</b>					
Yes	2	4.4	3	5.5	1.000
No	43	95.6	52	94.5	

**Figure 21: Bar graph showing comparison of skeletal anomalies in M and M + M group.**

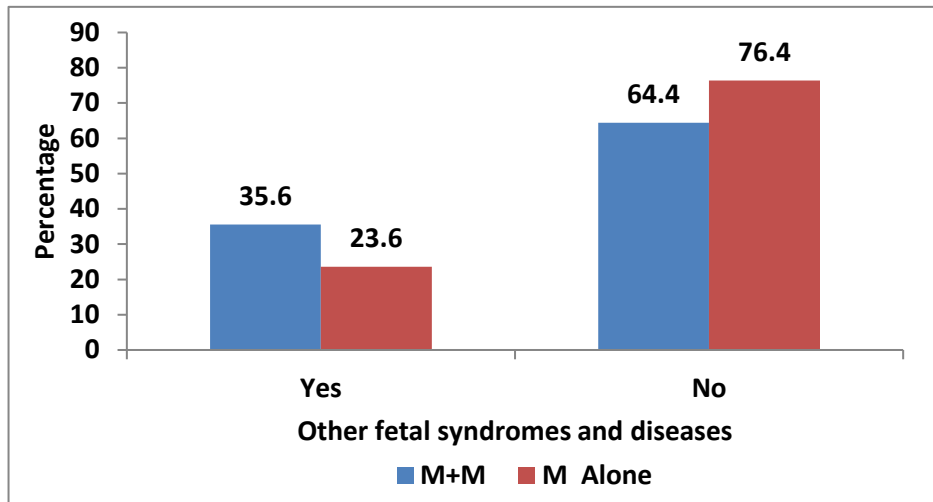


**Other anomalies, syndromes and other diseases**

**Table 18: Other anomalies, syndromes and other diseases**

<b>Groups</b>	<b>M + M</b>		<b>M alone</b>		<b>P - Value</b>
<b>Variables</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
<b>Fetal anomalies:</b>					
<b>Syndromes and other diseases</b>					
Yes	16	35.6	13	23.6	0.191
No	29	64.4	42	76.4	

**22: Bar graph showing comparison of other anomalies, syndromes and other diseases in M and M + M group.**

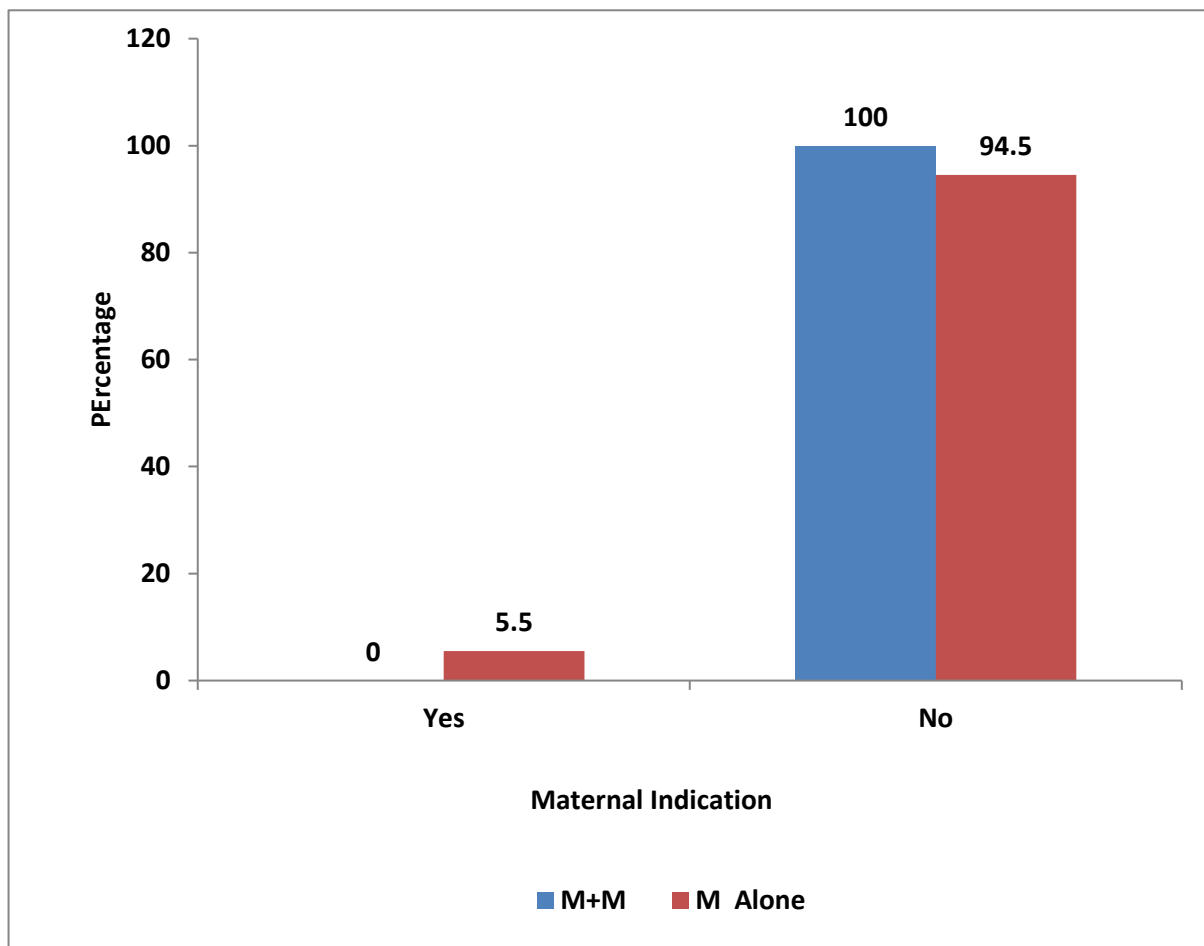


**Table 19: Comparison of indications for termination due to maternal indications in M and M + M group.**

Groups	M + M		M alone		P - Value
	n	%	n	%	
<b>Maternal indication</b>					
Yes	0	0.0	3	5.5	0.250
No	45	100.0	52	94.5	

Termination done for maternal indications were rectal carcinoma on chemotherapy, Ebstein anomaly and nephrotic syndrome with uncontrolled hypertension.

**Figure 23: Bar graph showing comparison of indications for termination due to maternal indications in M and M + M group.**

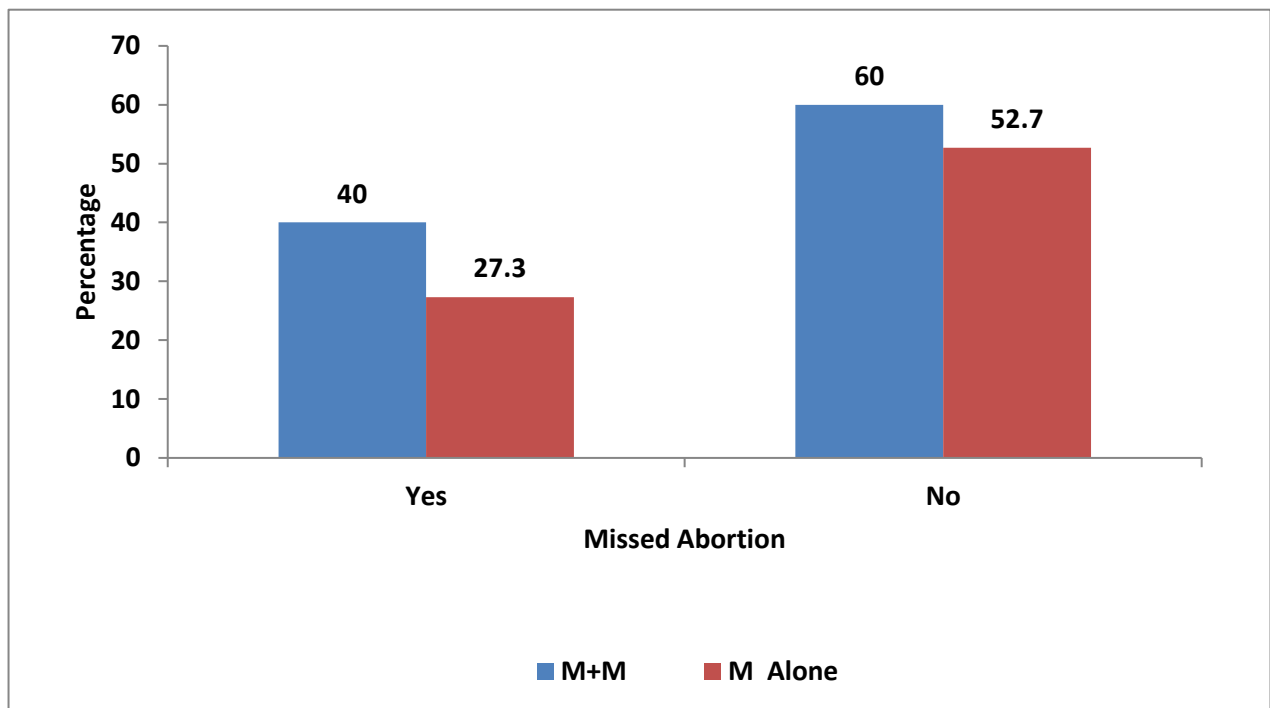


## Missed abortion

**Table 20: Comparison of indications for termination due to missed abortion in M and M + M group.**

<b>Groups</b>	<b>M + M</b>		<b>M alone</b>		<b>P - Value</b>
<b>Variables</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
<b>Missed abortion (MA)</b>					
Yes	18	40.0	26	27.3	0.466
No	27	60.0	29	52.7	

**Figure 24: Bar graph showing comparison of indications for termination due to missed abortion in M and M + M group.**



**Primary outcome - Induction Abortion Interval (IAI)**

The Induction Abortion Interval included in this study group was duration from first dose of misoprostol administration to complete expulsion

[IAI] in the M alone group was 19.86 hours and 13.08 hours in the combination group

which was statistically significant with a p-value of 0.005.

40.7 % of patients in the study had complete abortion within the first 12 hours of Misoprostol administration.

44.7% were from the combination group and 37.5% from the Misoprostol alone group expelled completely in the first 12 hours.

Complete abortion between 13 to 24 hours after misoprostol administration was found in 31 % of the patients in the study. Furthermore, 42.1% in the combination group and 31.3 % in the Misoprostol alone group aborted completely between 13 and 24 hours.

Women requiring more than 24 hours for complete abortions were 13.2 % in the combination group whereas 31.3% women took more than 24 hours for complete expulsion in the Misoprostol alone group.

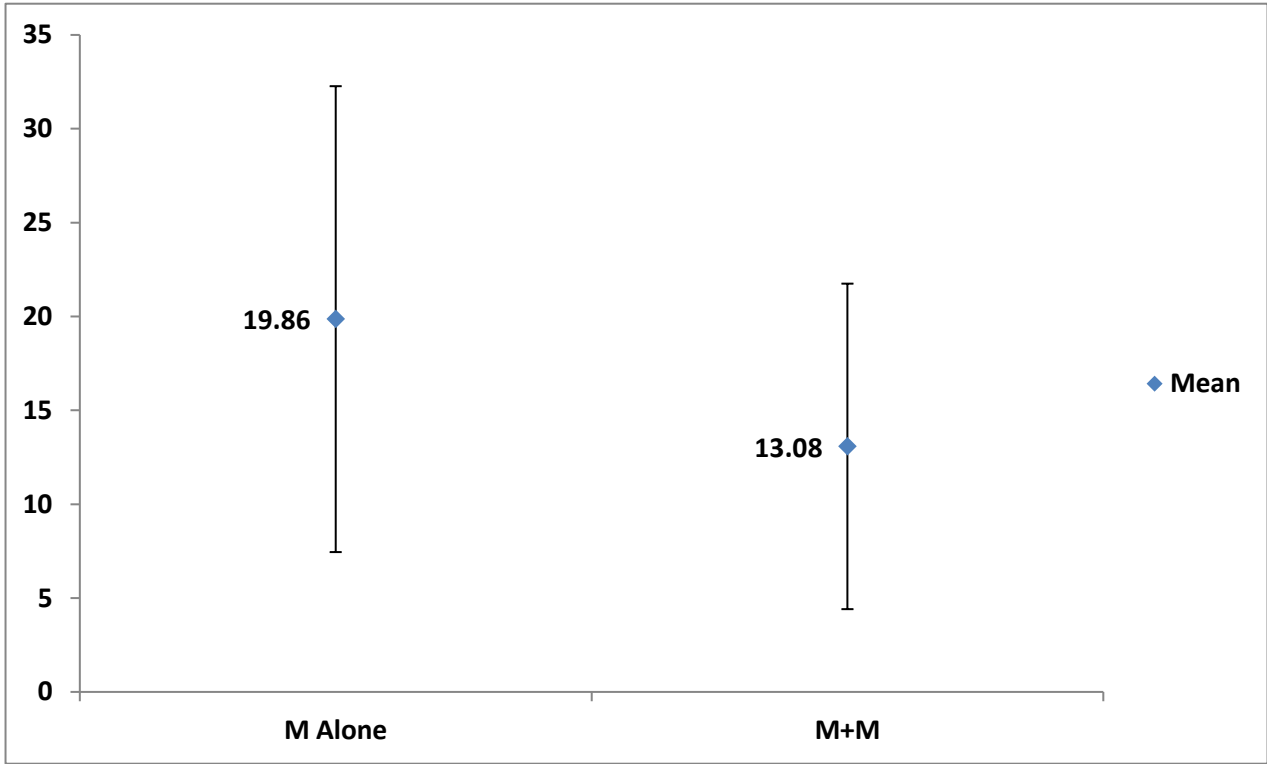
**Table 21: Comparison of Induction Abortion Interval (IAI) noted in**

**M and M + M group.**

<b>Groups</b>	<b>M alone</b>		<b>M + M</b>		<b>P value</b>
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>	
IAI (In hours)	19.86	12.41	13.08	8.67	0.005



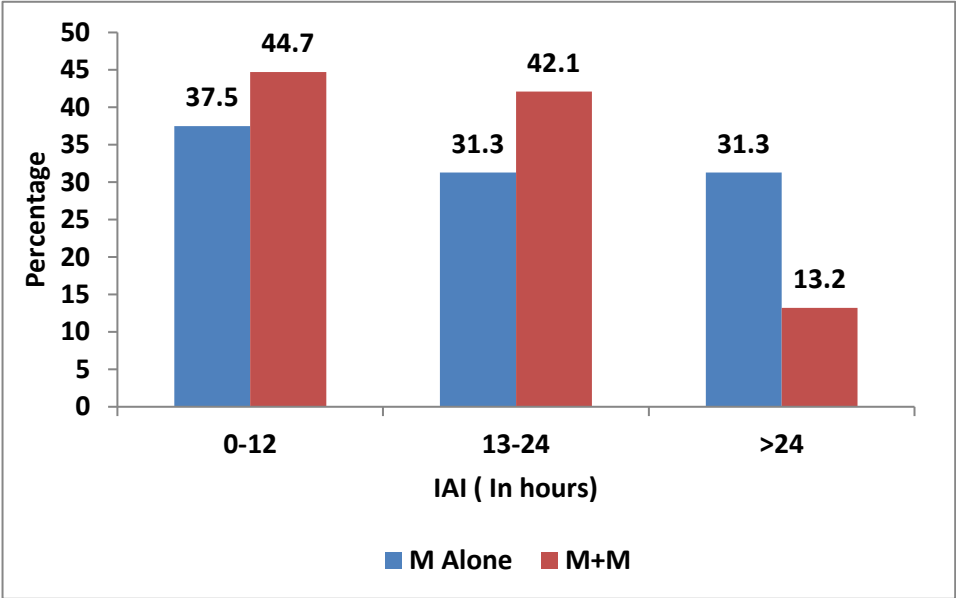
**Figure 25: Bar graph showing comparison of Induction Abortion Interval (IAI) noted in M and M + M group.**



**Table 22: Comparison of Induction Abortion Interval (IAI) noted according to duration in hours in M and M + M group**

<b>Groups</b>	<b>M alone</b>		<b>M + M</b>		<b>P value</b>
<b>Variables</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
<b>IAI in hours</b>					
0-12 hours	18	37.5	17	44.7	0.152
13-24 hours	15	31.3	16	42.1	
>24 hours	15	31.3	5	13.2	

**Figure 26: Bar graph showing comparison of Induction Abortion Interval (IAI) noted according to duration in hours in M and M + M group**



**IAI according to parity**

Nulliparous women required more time to abort completely than multiparous women

**Table 23: Comparison of Induction Abortion Interval (IAI) noted according to parity in M and M + M group**

Variable	IAI (In hours)							
	M+M				M alone			
	0-12	13-24	>24	P - Value	0-12	13-24	>24	P - Value
<b>Parity</b>								
0	7(41.2)	10(62.5)	2(40.0)	0.597	7(38.9)	10(66.7)	11(73.3)	0.181
1	6(35.3)	5(31.3)	2(40.0)		7(38.9)	3(20.0)	4(26.7)	
2	4(23.5)	1(6.3)	1(20.0)		4(22.2)	2(13.3)	0(0.0)	

### IAI according to gestational age

Women who had complete abortion up to 14 weeks gestation after combination regimen within 12 hours were 47.1% while in misoprostol group 44.4% number of women who aborted completely within 12 hours were of 15 to 17+6 weeks gestation.

**Table 24: Comparison of Induction Abortion Interval (IAI) noted according to parity in M and M + M group**

Variable	IAI (In hours)							
	M+M				M alone			
	0-12	13-24	>24	P - Value	0-12	13-24	>24	P - Value
<b>GA in weeks</b>								
12-14.6	8(47.1)	10(62.5)	2(40.0)	0.278	5(27.8)	8(53.3)	8(53.3)	0.118
15-17.6	6(35.3)	2(12.5)	3(60.0)		8(44.4)	2(13.3)	1(6.7)	
18-20	3(17.6)	4(25.0)	0(0.0)		5(27.8)	5(33.3)	6(40.0)	

In the combination group, 47.1 % of patients who expelled in the first 12 hours and 62.5 % of patients who expelled in between 13 to 24 hours were between 12 to 14+6 weeks

whereas 60% of those who took more than 24 hours to expel were between 15 to 17+6 weeks. In the Misoprostol only group, 44.4% who expelled in the first 12 hours were between 15 to 17+6 weeks gestation and 53.3% who expelled between 13 and 24 hours were between 12- and 14.6-weeks gestation.

### **Success rate**

57.8 % of participants in the combination group had complete abortion and 50.9 % in the Misoprostol alone group had complete abortion whereas 35.6 % in the combination group and 40 % in the Misoprostol alone group had incomplete abortion and thereby required surgical evacuation.

Out of the 8 women who had failed MTP, 5 had re-induction and expelled completely and 3 underwent surgical evacuation.

### **Secondary outcomes**

#### **I. Dosage and side effects of Misoprostol**

##### **1. Dosage of Misoprostol**

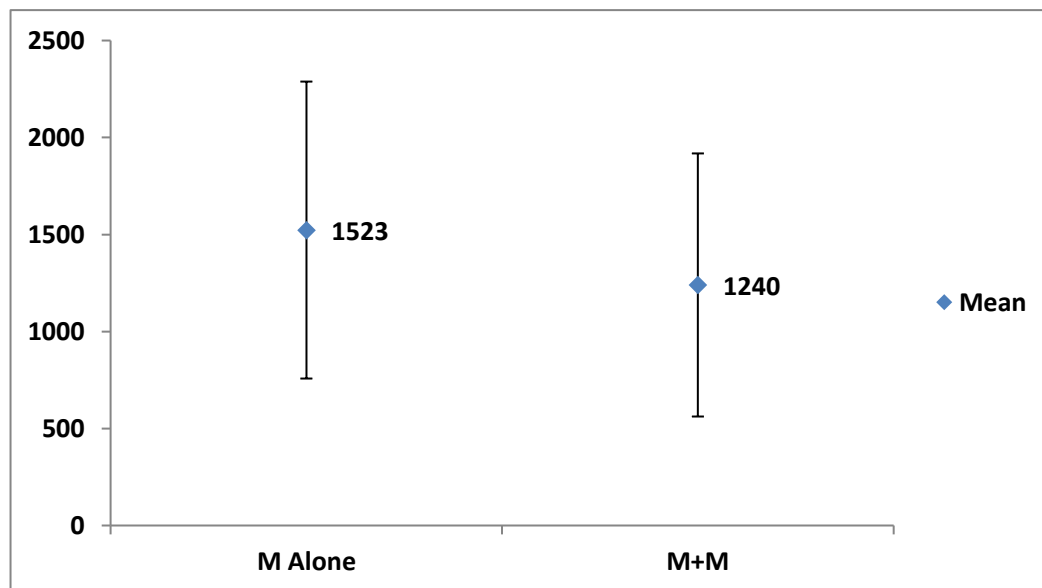
The mean of the total dosage of Misoprostol required for complete abortion in our study was 1.24 mg and 1.523 mg in the M alone group which was not statistically significant.

**1a. Total dose of Misoprostol used**

**Table 25: Comparison of total dose of Misoprostol used in M and M + M group**

Groups	M alone		M + M		P value
	Mean	SD	Mean	SD	
Total dose of Misoprostol used (in mcg)	1523	765.45	1240	678.16	0.068

**Figure 27: Comparison of total dose of Misoprostol used in M and M + M group**



### 1b. Number of doses of Misoprostol

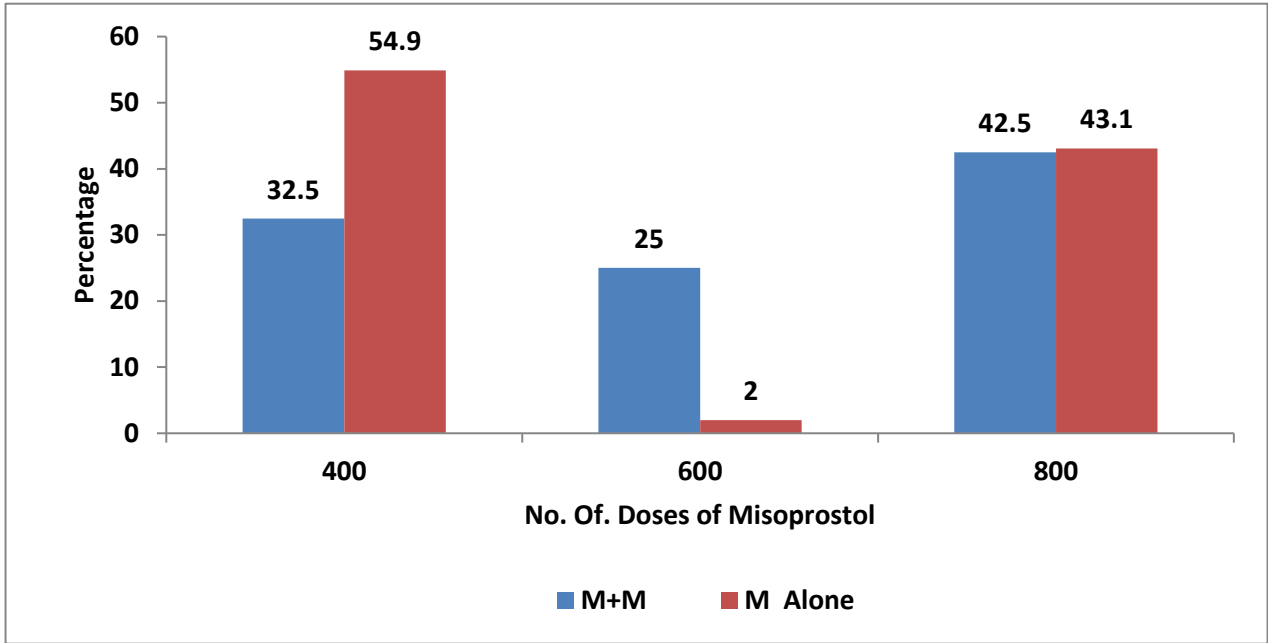
42.5 % of patients in the M+M group received 800 mcg of Misoprostol and 43.1 % of patients in the M alone group received 800 mcg of Misoprostol. 54.9 % of patients in the M alone group received 400 mcg Misoprostol whereas only 32.5% in the combination group received 400 mcg Misoprostol.

**Table 26: Comparison of number of doses of Misoprostol used in M and M + M group**

Groups	M + M		M alone		P - Value
	n	%	n	%	
<b>No. of doses of Misoprostol (in mcg)</b>					0.002
400	13	32.5	28	54.9	
600	10	25.0	1	2.0	
800	17	42.5	22	43.1	



**Figure 28: Bar graph showing comparison of number of doses of Misoprostol used in M and M + M group**



**2. Side effects of Misoprostol**

Side effects due to Misoprostol were noted to be less in the M + M group as compared to the Misoprostol alone group.

**Table 27: Comparison of side effects of Misoprostol noted in M and M + M group**

Variable	Group		P - Value
	M alone	M + M	
	n (%)	n (%)	
<b>Side effect</b>			
Nausea/vomiting	6 (10.9)	3(6.6)	0.01
Chills/Rigor	3(5.45)	2(4.4)	
Fever	5(9.09)	3(6.6)	
Diarrhoea	1(1.81)	0	

## **II. Need for re-induction**

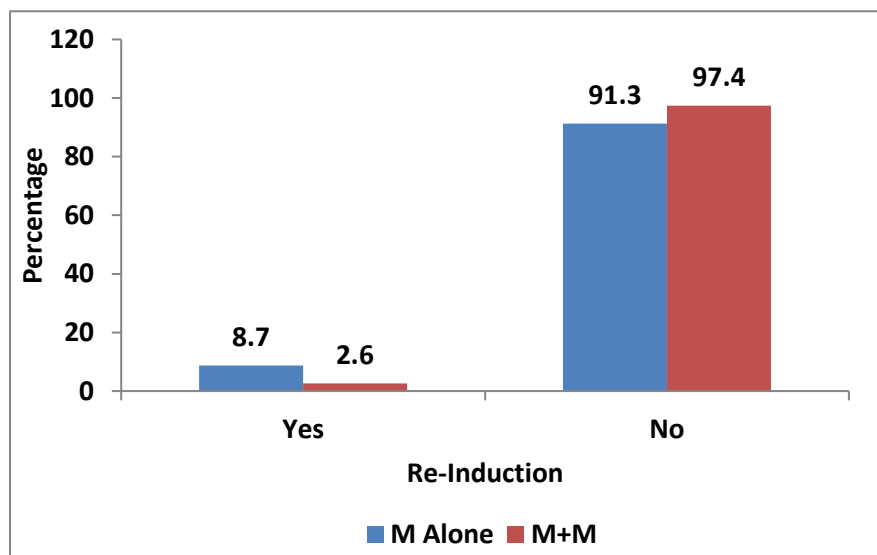
Re-induction -means Women who did not expel after medication and required repeat medication.

Four women required re-induction in the M alone group whereas one woman had reinduction in the M+M group.

**Table 28: Comparison of need for re-induction in M and M + M group**

Groups	M alone		M + M		P value
Variables	n	%	n	%	
<b>Re-induction</b>					
Yes	4	8.7	1	2.6	0.369
No	42	91.3	38	97.4	

**Figure 29: Bar graph showing comparison of need for re-induction in M and M + M group**



### III. Need for surgical evacuation

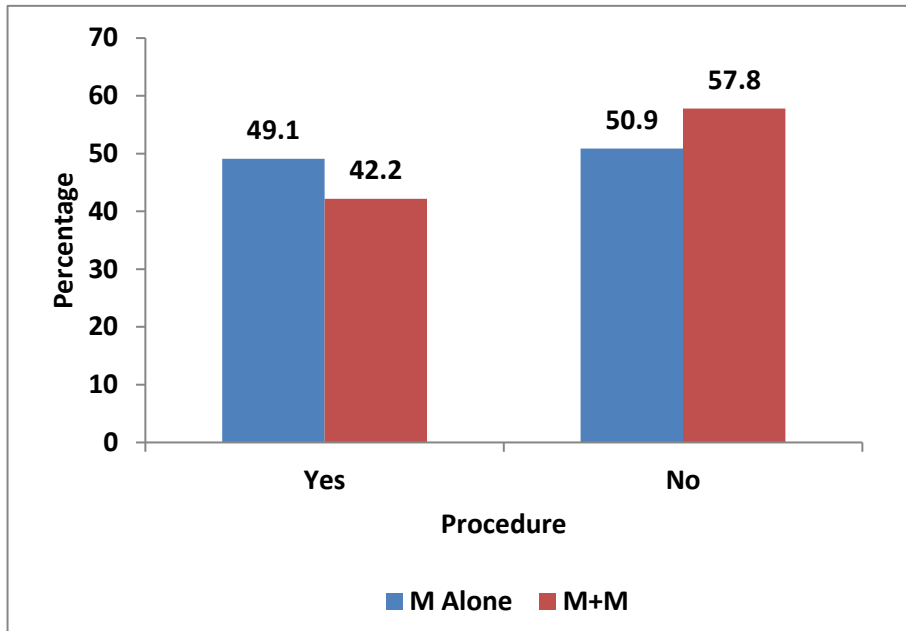
Total 46 women/100 in the study required additional surgical evacuation procedure.

On comparison of the 2 groups, 19 (42.2 %) of patients in the combination group required additional surgical evacuation whereas 27 (49.1%) patients in the M alone group.

**Table 29: Comparison of need for surgical evacuation in M and M + M group.**

Groups	M alone		M + M		P value
	n	%	n	%	
<b>Procedure done</b>					
Yes	27	49.1	19	42.2	0.493
No	28	50.9	26	57.8	

**Figure 30: Bar graph showing comparison of need for surgical evacuation in M and M + M group.**



#### **IV. Complications**

Excessive bleeding was seen in 15 women (31.9%). Out of this, 5 were from the combination group and 10 from the M alone group.

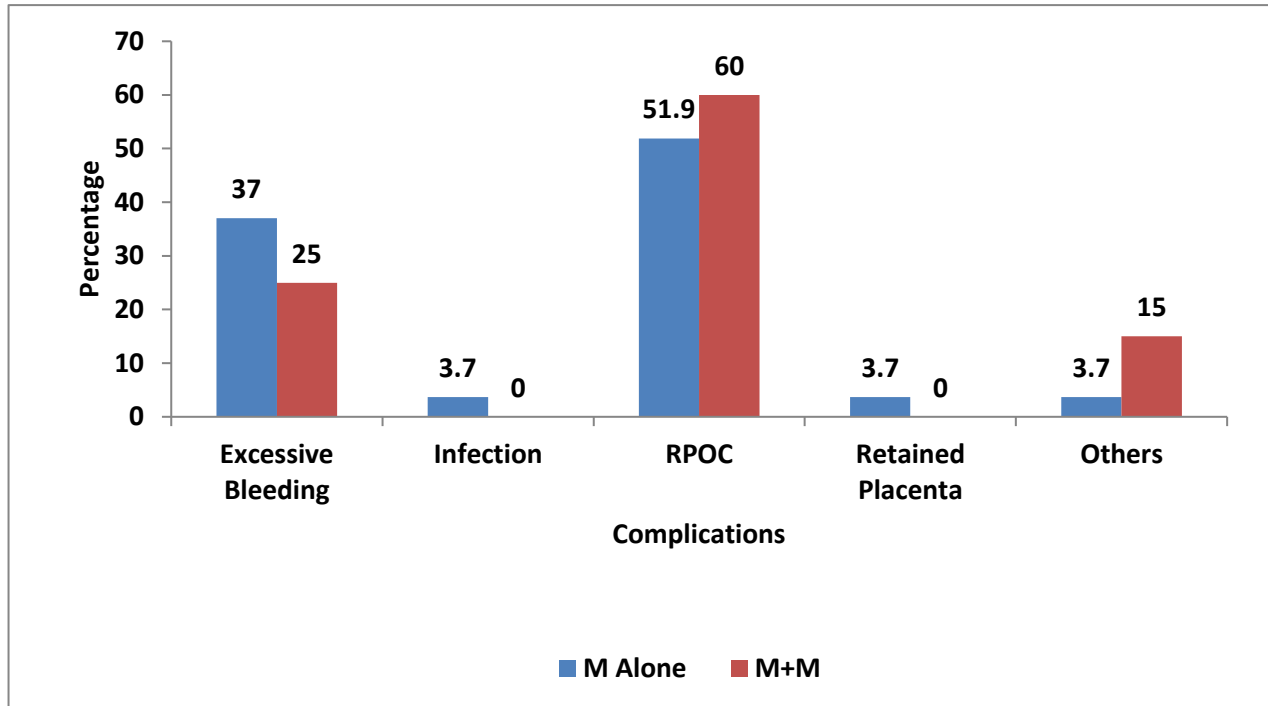
Retained products of conception were noted in 26 (55.3 %) women in the study

12 participants were from the combination group and 14 patients were from the M alone group

**Table 30: Comparison of complications noted in M and M + M group.**

<b>Groups</b>	<b>M alone</b>		<b>M + M</b>		<b>P value</b>
<b>Variables</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
<b>Complications</b>					
Excessive	10	37.0	5	25.0	0.446
Bleeding	1	3.7	0	0.0	
Infection	14	51.9	12	60.0	
RPOC	1	3.7	0	0.0	
Retained	1	3.7	3	15.0	
Placenta					

**Figure 31: Bar graph showing comparison of complications noted in M and M + M group.**



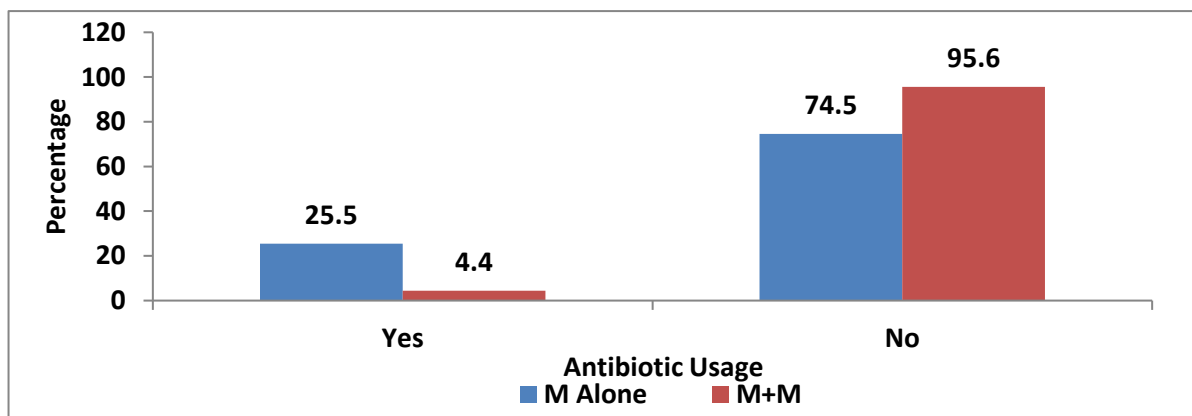
### **V. Need for antibiotic use**

16/100 patients required usage of antibiotics out of which only 2 were from the M+M group whereas 14 were from the M alone group.

**Table 31: Comparison of need for antibiotics noted in M and M + M group.**

Groups	M alone		M + M		P value
	n	%	n	%	
<b>Antibiotic Use</b>					
Yes	14	25.5	2	4.4	0.004
No	41	74.5	43	95.6	

**Figure 32: Bar graph showing comparison of need for antibiotics noted in M and M + M group.**





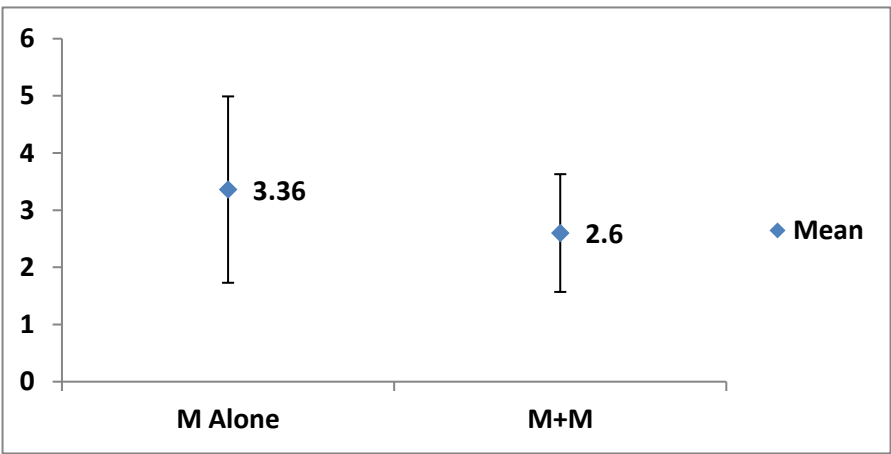
**IV. Duration of hospital stay**

The mean number of days of hospital stay in the M+M group was 2.6 and 3.36 in the M alone group and the difference was statistically significant with a p value of 0.01.

**Table 32: Comparison of duration of hospital stay noted in M and M + M group.**

Groups	M alone		M + M		P value
	Mean	SD	Mean	SD	
Duration of hospital stay (Days)	3.36	1.63	2.60	1.03	0.010

**Figure 33: Comparison of duration of hospital stay noted in M and M + M group.**



## VI. Total amount of expenditure

The mean of the total bill amount in the combination group was Rs. 11026 whereas in the Misoprostol alone group it was Rs. 14614. This was statistically significant with a p-value of 0.035

**Table 33: Comparison of total amount of expenditure in M and M + M group.**

Variable	Mean SD	Median (IQR)	P -Value
Expenditure in Rupees			
M + M	11026.72 ± 8331.85	8000 (6335.0, 13120.0)	0.035
M alone	14614.85 ± 10397.74	12045 (7199.5, 19063.0)	

## **DISCUSSION**

Various studies have shown that the combined use of Mifepristone and Misoprostol reduces the induction to abortion interval in abortions. However, for the mid-trimester medical abortions, a standard protocol has not been available till date. Combination regimes have been recommended with Mifepristone dose as low as 200 mg. Vaginal Misoprostol has been recommended over other routes (36).

Misoprostol has already been proved to be efficacious in second trimester abortions. Numerous routes of administration have been in practice i.e., sublingual, oral and vaginal. Different regimens have been used and the induction abortion intervals for these regimens range from 12 hours to as high as 33 hours. However, combining Mifepristone with misoprostol for termination of first trimester pregnancy is now a widely used method. Mifepristone sensitizes the uterine myometrium and increases its sensitivity to prostaglandins. It acts by antagonizing the action of progesterone by binding with the progesterone receptors and thereby affecting prostaglandin synthesis and metabolism. It increases the production and decreases the deactivation of prostaglandins. Cervical softening is also induced by it and hence it enhances the efficacy of the prostaglandins in abortions (37).

In developing countries like India, especially in rural areas, termination of pregnancy in the second trimester is still a complicated procedure. The search for an ideal method which is safe, cheap and reliable needs emphasis. The combination

regimen of oral mifepristone 200 mg with vaginal misoprostol is an efficacious and non-invasive regimen for medical management of second trimester abortions. It brings a drastic difference in the induction to abortion interval and is associated with lesser side effects and good patient compliance. The side effects observed were actually directly proportional to the dosage of misoprostol. In settings where facilities for surgical termination of pregnancy are not available like primary health centres or outpatient clinics, this method can be used. The doctors with lack of expertise in surgical evacuation can also use this procedure for TOPs. If any complications arise, as in excessive bleeding per vaginum, retained products of conception, failed MTP, they can refer the patient to higher centres with facilities and expertise for surgical evacuation (38).

#### **Main finding of our study and comparison with previous studies**

Our prospective study compared the efficacy of Misoprostol alone over Mifepristone with Misoprostol combination and found that the combination regimen has high 24-hour success rate and is safe for second trimester TOPs thereby providing further evidence and supporting prior research on this topic. This study provides data on the medically performed TOPs at our Centre. A total of 100 patients were recruited in the study out of which 45 were in the mifepristone plus misoprostol group and 55 were in the misoprostol alone group.

## **Induction Abortion Interval**

The primary outcome in our study was the induction abortion interval. The IAI was significantly lesser in the combination group. The combination group had an IAI of 38 hours as compared to 48 hours in the Misoprostol alone group (p-value of 0.05). Borgatta and Kapp et al (39) and Dickinson et al (21) had similar outcomes in their studies. In yet another similar study, Nagaria et al (37) also reported a significantly shorter mean IAI interval.

According to Ngoc et al. the mean IAI reported the IAI as 8.1 h in the Mifepristone plus Misoprostol group and 10.6 h in the Misoprostol group alone which was statistically significant with a p value of 0.01 (40). Rasha et al in their study also reported a significantly lower mean IAI in the Mifepristone group ( $10.4 \pm 6.8$  h) as compared to the mean IAI of the Misoprostol alone group ( $20.6 \pm 9.7$  h) (36). The low induction to abortion interval is likely to make the combination regime more acceptable in women (30).

## **Induction Abortion Interval in relation to parity and gestational age**

In our study, the IAI was maximum in nulliparas in both the study groups and was least in multiparas. It was also noted that women the IAI was lower in women with lower gestational age. In the combination group, 47.1 % of patients who expelled in the first 12 hours and 62.5 % of patients who expelled in between 13 to 24 hours were of gestational age group 12 -14+6 weeks whereas in the Misoprostol only group, 44.4% who expelled in

the first 12 hours were between 15 to 17+6 weeks gestation and 53.3% who expelled between 13 and 24 hours were between 12- and 14+6-weeks gestation.

Also, the Misoprostol dose required were lower in primigravidae and women with lower gestational age. Heini et al in their study reported a similar finding and showed that the multigravida and women with early gestation completed faster (41).

In Mentula et al's study the median IAI and the median number of misoprostol doses required was lower in the combination group (42). The median IAI was noticed to be longer as gestational age increased and also in primigravidae. This leads us to speculate that sensitizing the myometrium is important in case of women with gestation more than 16 weeks because they are at risk of longer IAI.

Elami et al. in their study showed that the mean IAI was  $7.7 \pm 6$  hours in women with gestation greater than 19 weeks and it was  $11.2 \pm 6.9$  hours in women with less than 19 weeks gestation. Also, the IAI was longer in nulligravidae ( $12.4 \pm 10.3$  hours) as compared to multigravidae ( $7.9 \pm 7$  hours) (43).

Ashok et al found that the induction-to-abortion time of women with no previous vaginal deliveries is longer (44).

### **Success rate**

In our study, 86.8 % of participants in the combination group and 68.8 % of participants from the Misoprostol alone group had complete abortion within the first 24 hours of Misoprostol administration. 44.7% of participants from the combination group

and 37.5% of participants from the Misoprostol alone group expelled completely in the first 12 hours of Misoprostol administration.

57.8 % of participants in the combination group had complete abortion and 50.9 % in the Misoprostol alone group whereas 35.6 % in the combination group and 40 % in the Misoprostol alone had incomplete abortion and thereby required surgical evacuation.

Another 42.1% in the combination group and 31.3 % in the Misoprostol alone group aborted completely between 13 and 24 hours of Misoprostol administration. In their study, Hou et al. reported that 95–100 % aborted within 24 hours and the mean expulsion time was shorter in multiparous women ( $6.3 \pm 3.7$  h) (45). Borgatta and Kapp et al. (39), Elami et al. (43) and Dickinson et al.(21) also reported success rate of 95 % in the first 24 hours.

### **Dose and side-effects of Misoprostol used**

The mean dose of misoprostol used in the combination group was lower (1240 mcg) as compared to Misoprostol alone group (1523 mcg) though not statistically significant. This may be due to the fact that majority of patients in the combination group were between 12 to 17.6 weeks and received higher dose of Misoprostol whereas 30.9% in the Misoprostol alone group were between 18 to 20 weeks and have received lower doses of Misoprostol as per FIGO guidelines.

Other similar studies reported a statistically significant lower mean dose for the

combination group as compared to the misoprostol group. In the study by Nagaria et al (37), the mean dose of misoprostol in the combination group was lesser as compared to the Misoprostol alone group.

42.5 % and 43.1 % of women in the M+M group and the M alone group received 800 mcg of Misoprostol respectively. On the other hand, 54.9 % of patients in the M alone group received 400 mcg Misoprostol whereas only 32.5% in the combination group received 400 mcg Misoprostol.

It has also been noted in many studies that shortest induction-to-abortion interval and the highest success rate maybe be related to the misoprostol dose. 600–800-mcg initiation dose of misoprostol has been associated with the highest 24-hr success rate of 97–100% whereas when 400-mcg of Misoprostol is used as the starting dose, the success rate within 24 hours is 91–94%. When the 200-mcg of Misoprostol is used as the initiation dose, the 24-hour success rate is the lowest (66–75%) as noted in some studies.

Furthermore, the IAI may also be related to the starting misoprostol dose. When misoprostol starting dose is 600–800 mcg, the IAI has been noted to be 5 hours by Chai et al, while the IAI is 7 hours and 10 hours for Misoprostol doses of 400 and 200 mcg by Hou et al (45).

In a review article by Wildschut et al. suggested that mifepristone plus misoprostol is the most efficient regimen among medical methods for second trimester terminations and that Misoprostol when administered 3 hourly is more effective than



when administered 6-hourly. This is explained by the fact that the action of misoprostol is enhanced by Mifepristone and thereby reducing the IAI and dosage of misoprostol used (46).

### **Side effects**

Nausea, vomiting, febrile illness and diarrhoea like side effects were seen more often in the Misoprostol alone group than the combination group. This can be explained due to the greater dosage of Misoprostol required and the prolonged induction abortion interval.

### **Need for surgical evacuation**

46 percent of patients in the study required additional surgical evacuation procedure. Out of this, 38 percent was due to incomplete abortion and 8 percent had failed medical method.

However, on comparison of the 2 groups, only 19 (42.2 %) of women in the combination group required additional surgical evacuation whereas 27 (49.1%) patients in the M alone group needed surgical evacuation.

The need for surgical evacuation was high in the Misoprostol alone group as compared to the combination group. The dosing of misoprostol may also affect the rate of surgical evacuation. Earlier Surgical evacuation used to be a routine procedure following all second trimester medical TOPs. In the present study the criteria for evacuation were similar between the two groups. The misoprostol doses were administered Q12H or Q6H

in both the groups based on the gestation as per FIGO guidelines. These differences may have an effect on the rate of surgical evacuation.

### **Complications**

Number of patients with complications were more in the Misoprostol alone group. The most common complication was retained products of conception. 26 (55.3 %) women in the study had retained products of conception of which 12 women were from the combination group and 14 were from the M alone group.

15 (31.9%) patients had excessive bleeding during journey of medical abortion. Out of this, 10 from the M alone group vs 5 were from the combination group.

### **The need for antibiotic usage**

16 women in the study required antibiotics because of febrile illness. Out of which 14 were from the Misoprostol alone group and 2 were from the combination group which was statistically significant with a p-value of 0.004.

### **Financial burden**

There was also difference in the financial burden as assessed by the number of days and duration of hospital stay. The hospital stay was longer in the Misoprostol alone group than the combination group. The mean number of days of hospital stay in the M+M group was approximately 2 days and more than 3.3 days in the M alone group which was noted as statistically significant [p-value of 0.01].

Total expense paid in the combination group was Rs. 11026 whereas in the Misoprostol alone group it was Rs. 14614. showed statistically significance with a p-value of 0.035.

### **Limitations of the study**

The limitations of this study are:

1. Non-randomised nature, as the choice of management strategy depended upon patient situation rather than randomisation.
2. Small sample size.

### **Strengths of the study**

The strength of this study is its prospective nature with broader range of clinically relevant outcomes as compared to other retrospective studies on this topic.

### **SUMMARY**

This study aimed to compare the efficacy of Mifepristone with Misoprostol regimen with the Misoprostol alone regimen in termination of pregnancy between 12- and 20-weeks gestation. The primary objective of the study was to compare the induction abortion interval (IAI) of both the regimens. The secondary outcomes were to determine the maximum dosage and frequency of Misoprostol required for complete abortion, to assess the need for surgical evacuation with these 2 medical regimens, to compare side

effects and complications and to compare the cost effectiveness (the impacts of the two regimes in the length of hospital stay and cost of treatment).

A total of 100 women were recruited for the study over a span of 10 months (from January 2021 to October 2022) out of which 55 belonged to the Misoprostol alone group and 45 belonged to the Mifepristone + Misoprostol group. Data was collected and analyzed using SPSS software.

We found the following results:

- 1) The induction abortion interval was lesser in the combination group as compared to the Misoprostol alone group and was statistically significant ( $p < 0.005$ ). The IAI in the combination group was 13.08 hours and the IAI in the Misoprostol alone group was 19.86 hours.
- 2) The dosage of Misoprostol required in complete abortion was also lower in the combination group (1240 mcg) as compared the Misoprostol alone group (1523 mcg) with a p value of 0.068.
- 3) The need for surgical evacuation was lesser in the combination regimen as compared to the Misoprostol alone group though not statistically significant. Only 19 women in the combination group underwent surgical evacuation whereas 27 women from the misoprostol alone group underwent surgical evacuation.
- 4) Complications and side-effects of Misoprostol were lesser in the combination group as the total dosage of Misoprostol required in this group was less as compared to the Misoprostol

alone group.

- 5) The number of days of hospital stay was lesser in the combination group (2.6 days) than in the Misoprostol alone group (3.36 days) and was statistically significant with a p value of 0.01. Total expense paid in the combination group was Rs. 11026 whereas in the Misoprostol alone group it was Rs. 14614 which was statistically significant with a p-value of 0.035.

Table 34: Composite results of the study

<b>Groups</b>	<b>M + M</b>		<b>M alone</b>		<b>P - Value</b>
<b>Variables</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
<b>Age in Years</b>					
< 20	5	11.1	4	7.3	0.108
20-25	9	20.0	17	30.9	
26-30	14	31.1	24	43.6	
>30	17	37.8	10	18.2	
<b>Parity</b>					
0	23	51.1	32	58.2	0.711
1	15	33.3	17	30.9	
2	7	15.6	6	10.9	
<b>GA TOP (in weeks)</b>					
12-14.6	24	53.3	25	45.5	0.196
15-17.6	14	31.1	13	23.6	
18-20	7	15.6	17	30.9	
<b>Previous h/o Abortions</b>					
Yes	16	35.6	20	36.4	0.933
No	29	64.4	35	63.6	

Table 35: Termination of pregnancy planned according to earlier scans

<b>Groups</b>	<b>M + M</b>		<b>M alone</b>		<b>P - Value</b>
<b>Variables</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
<b>Fetal anomalies:</b>					
CNS	8	17.8	8	14.5	0.661
CVS	4	8.9	4	7.3	1.000
Renal	0	0	3	5.5	0.250
Skeletal	2	4.4	3	5.5	1.000
Others					

	16	35.6	13	23.6	0.191
<b>Maternal indication</b>	0	0	3	5.5	0.250
<b>Missed abortion (MA)</b>	18	40.0	26	27.3	0.466

Table 36 Outcomes

<b>Groups</b>	<b>M alone</b>		<b>M + M</b>		<b>P value</b>
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>	
<b>Variables</b>					
IAI (in hours)	19.86	12.41	13.08	8.67	0.005
Dosage of Misoprostol (mcg)	1523	765.45	1240	678.16	0.068
<b>Re-induction</b>					
Yes	4	8.7	1	2.6	0.369



No	42	91.3	38	97.4	
Duration of hospital stay (Days)	3.36	1.63	2.60	1.03	0.010

Variable	Mean SD	Median (IQR)	P -Value
<b>Expenditure (in Rupees)</b>			
M + M	11026.72 ± 8331.85	8000 (6335.0, 13120.0)	0.035
M alone	14614.85 ± 10397.74	12045 (7199.5, 19063.0)	

## CONCLUSION

Adding mifepristone to misoprostol in second trimester abortion regimens gives a definite advantage.

The combination of mifepristone and misoprostol regimen gives the following advantages as noted in the study:

1. The induction abortion interval is significantly reduced when Mifepristone is added to Misoprostol.
2. The dosage of Misoprostol required in complete abortion was lower

3. The need for surgical evacuation was lesser
4. Complications and side-effects of Misoprostol were lesser
5. May give financial benefit by the shorter duration of hospital stay.

Therefore, efforts should be made for its availability globally for its use in the second trimester.

## **BIBLIOGRAPHY**

1. Current and potential methods for second trimester abortion | Elsevier Enhanced Reader [Internet]. [cited 2021 May 21]. Available from:  
<https://reader.elsevier.com/reader/sd/pii/S1521693419300495?token=295DE8ABB6665E09BE84E52EE8E4A2EF7A96DAA1D47991AB2EE70172B334C42B5448257C11820ECF07015ABCC05433A2&originRegion=eu-west-1&originCreation=20210521092432>
2. Kapp N, Andersen K, Griffin R, Handayani AP, Schellekens M, Gomperts R. Medical abortion at 13 or more weeks gestation provided through telemedicine: A retrospective review of services. *Contracept X* [Internet]. 2021 Jan 25 [cited 2021 May 21];3. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7881210/>
3. Garfield RE, Baulieu EE. 10 The antiprogesterone steroid RU 486: a short pharmacological and clinical review, with emphasis on the interruption of pregnancy. *Baillières Clin Endocrinol Metab* [Internet]. 1987 Feb [cited 2021 Nov 13];1(1):207–21. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0950351X87800599>
4. Grossman D, White K, Harris L, Reeves M, Blumenthal PD, Winikoff B, et al. Continuing pregnancy after mifepristone and “reversal” of first-trimester medical abortion: a systematic review. *Contraception* [Internet]. 2015 Sep [cited 2021 Nov 13];92(3):206–11. Available from:  
<https://linkinghub.elsevier.com/retrieve/pii/S0010782415002267>

5. Chen C, Lin F, Wang X, Jiang Y, Wu S. Mifepristone combined with ethacridine lactate for the second-trimester pregnancy termination in women with placenta previa and/or prior cesarean deliveries. *Arch Gynecol Obstet* [Internet]. 2017 Jan [cited 2021 Nov 14];295(1):119–24. Available from: <http://link.springer.com/10.1007/s00404-016-4205-8>
6. Sedgh G, Bearak J, Singh S, Bankole A, Popinchalk A, Ganatra B, et al. Abortion incidence between 1990 and 2014: global, regional, and subregional levels and trends. *The Lancet* [Internet]. 2016 Jul [cited 2021 Nov 13];388(10041):258–67. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0140673616303804>
7. Yokoe R, Rowe R, Choudhury SS, Rani A, Zahir F, Nair M. Unsafe abortion and abortion-related death among 1.8 million women in India. *BMJ Glob Health* [Internet]. 2019 May [cited 2021 Nov 13];4(3):e001491. Available from: <https://gh.bmj.com/lookup/doi/10.1136/bmjgh-2019-001491>
8. Lalitkumar S, Bygdeman M, Gemzell-Danielsson K. Mid-trimester induced abortion: a review. *Hum Reprod Update* [Internet]. 2007 Jan 1 [cited 2021 Nov 13];13(1):37–52. Available from: <http://academic.oup.com/humupd/article/13/1/37/751686/Midtrimester-induced-abortion-a-review>
9. Prata N, Sreenivas A, Vahidnia F, Potts M. Saving maternal lives in resource-poor settings: Facing reality. *Health Policy* [Internet]. 2009 Feb [cited 2021 Nov

13];89(2):131–48. Available from:

<https://linkinghub.elsevier.com/retrieve/pii/S016885100800122X>

10. MTP ACT, 1971 | Ministry of Health and Family Welfare | GOI [Internet]. [cited 2021 Aug 22]. Available from: <https://main.mohfw.gov.in/acts-rules-and-standards-health-sector/acts/mtp-act-1971>
11. India’s amended law makes abortion safer and more accessible [Internet]. [cited 2021 Aug 19]. Available from: <https://www.who.int/india/news/detail/13-04-2021-india-s-amended-law-makes-abortion-safer-and-more-accessible>
12. Watkinson G, Hopkins A, Akbar FA. The therapeutic efficacy of misoprostol in peptic ulcer disease. *Postgrad Med J.* 1988;64 Suppl 1:60–77.
13. Brunton LL, Knollmann BC, Hilal-Dandan R. Goodman & Gilman’s: : The Pharmacological Basis of Therapeutics / [Internet]. New York, N.Y.: McGraw-Hill Education LLC.; 2018 [cited 2021 Aug 24]. Available from: <https://go.openathens.net/redirector/touro.edu?url=http://accessmedicine.mhmedical.com/book.aspx?bookid=2189>
14. Misoprost-200 Tablet 4’s Price, Uses, Side Effects, Composition [Internet]. Apollo Pharmacy. [cited 2021 Dec 21]. Available from: <https://www.apollopharmacy.in/medicine/misoprost-200mcg-tablet>

15. Misoprostol. In: Wikipedia [Internet]. 2021 [cited 2021 Dec 21]. Available from:  
<https://en.wikipedia.org/w/index.php?title=Misoprostol&oldid=1060036840>
16. Allen R, O'Brien BM. Uses of Misoprostol in Obstetrics and Gynecology. *Rev Obstet Gynecol* [Internet]. 2009 [cited 2021 Aug 22];2(3):159–68. Available from:  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2760893/>
17. mapmiso\_\_en.pdf [Internet]. [cited 2021 Dec 21]. Available from:  
[https://www.redaas.org.ar/archivos-recursos/mapmiso\\_\\_en.pdf](https://www.redaas.org.ar/archivos-recursos/mapmiso__en.pdf)
18. Nautiyal D, Mukherjee K, Perhar I, Banerjee N. Comparative Study of Misoprostol in First and Second Trimester Abortions by Oral, Sublingual, and Vaginal Routes. *J Obstet Gynaecol India* [Internet]. 2015 Jul [cited 2021 Nov 13];65(4):246–50. Available from:  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4518018/>
19. Wood SL, Brain PH. Medical management of missed abortion: a randomized clinical trial. *Obstet Gynecol* [Internet]. 2002 Apr 1 [cited 2021 Nov 14];99(4):563–6. Available from: <https://www.sciencedirect.com/science/article/pii/S0029784401017653>
20. Figure 1. Mean plasma concentrations of misoprostol acid over time... [Internet]. ResearchGate. [cited 2021 Dec 21]. Available from:  
[https://www.researchgate.net/figure/Mean-plasma-concentrations-of-misoprostol-acid-over-time-arrowbars-1-SD\\_fig1\\_11539375](https://www.researchgate.net/figure/Mean-plasma-concentrations-of-misoprostol-acid-over-time-arrowbars-1-SD_fig1_11539375)

21. Dickinson JE, Jennings BG, Doherty DA. Mifepristone and Oral, Vaginal, or Sublingual Misoprostol for Second-Trimester Abortion: A Randomized Controlled Trial. *Obstet Gynecol* [Internet]. 2014 Jun [cited 2021 Jun 2];123(6):1162–8. Available from: [https://journals.lww.com/greenjournal/Fulltext/2014/06000/Mifepristone\\_and\\_Oral,\\_Vaginal,\\_or\\_Sublingual.4.aspx](https://journals.lww.com/greenjournal/Fulltext/2014/06000/Mifepristone_and_Oral,_Vaginal,_or_Sublingual.4.aspx)
22. PubChem. Mifepristone [Internet]. [cited 2021 Aug 30]. Available from: <https://pubchem.ncbi.nlm.nih.gov/compound/55245>
23. Mifepristone abortion inducing drug, chemical structure. also used as emergency contraceptive agent. atoms are represented as | CanStock [Internet]. [cited 2021 Dec 21]. Available from: <https://www.canstockphoto.com/mifepristone-abortion-inducing-drug-15643862.html>
24. Mifepristone + Misoprostol tablets - Google ಹುಡುಕಾಟ [Internet]. [cited 2021 Dec 21]. Available from: [https://www.google.com/search?q=Mifepristone+%2B+Misoprostol+tablets&source=lnms&tbm=isch&sa=X&ved=2ahUKEwj7nvib-PT0AhWiSWwGHYwnCscQ\\_AUoAXoECAEQAw&biw=1034&bih=588&dpr=1#imgrec=6CjxOYQVVyrLLM](https://www.google.com/search?q=Mifepristone+%2B+Misoprostol+tablets&source=lnms&tbm=isch&sa=X&ved=2ahUKEwj7nvib-PT0AhWiSWwGHYwnCscQ_AUoAXoECAEQAw&biw=1034&bih=588&dpr=1#imgrec=6CjxOYQVVyrLLM)
25. Countries where Mifepristone is available - Google ಹುಡುಕಾಟ [Internet]. [cited 2021 Dec 21]. Available from:

[https://www.google.com/search?q=Countries+where+Mifepristone+is+available&source=lnms&tbm=isch&sa=X&ved=2ahUKEwixhuaw-fT0AhVPyzgGHfiDBbcQ\\_AUoAXoECAEQAw&biw=1034&bih=588&dpr=1#imgrc=azjAocqT2RG5GM](https://www.google.com/search?q=Countries+where+Mifepristone+is+available&source=lnms&tbm=isch&sa=X&ved=2ahUKEwixhuaw-fT0AhVPyzgGHfiDBbcQ_AUoAXoECAEQAw&biw=1034&bih=588&dpr=1#imgrc=azjAocqT2RG5GM)

26. Urquhart DR, Templeton AA. The use of mifepristone prior to prostaglandin-induced mid-trimester abortion. *Hum Reprod* [Internet]. 1990 Oct [cited 2021 Nov 15];5(7):883–6. Available from: <https://academic.oup.com/humrep/article/669378/The>
27. Platais I, Tsereteli T, Maystruk G, Kurbanbekova D, Winikoff B. A prospective study of mifepristone and unlimited dosing of sublingual misoprostol for termination of second-trimester pregnancy in Uzbekistan and Ukraine. *BMJ Sex Reprod Health* [Internet]. 2019 Jul [cited 2021 Aug 19];45(3):177–82. Available from: <http://jfprhc.bmj.com/lookup/doi/10.1136/bmjsex-2018-200167>
28. Prodan N, Breisch J, Hoopmann M, Abele H, Wagner P, Kagan KO. Dosing interval between mifepristone and misoprostol in second and third trimester termination. *Arch Gynecol Obstet* [Internet]. 2019 Mar [cited 2021 Jun 2];299(3):675–9. Available from: <http://link.springer.com/10.1007/s00404-018-5017-9>
29. Shochet T, Dragoman M, Blum J, Abbas D, Louie K, Platais I, et al. Could second-trimester medical abortion be offered as a day service? Assessing the feasibility of a 1-day outpatient procedure using pooled data from six clinical studies. *Contraception*



[Internet]. 2019 May [cited 2021 May 21];99(5):288–92. Available from:

<https://linkinghub.elsevier.com/retrieve/pii/S0010782419300083>

30. Dabash R, Chelli H, Hajri S, Shochet T, Raghavan S, Winikoff B. A double-blind randomized controlled trial of mifepristone or placebo before buccal misoprostol for abortion at 14-21 weeks of pregnancy. *Int J Gynecol Obstet* [Internet]. 2015 Jul [cited 2021 Aug 19];130(1):40–4. Available from:  
<http://doi.wiley.com/10.1016/j.ijgo.2015.02.023>
31. Kaur M, Kaur H, Sharma S, Mangla M. Mifepristone followed by Misoprostol for Mid trimester Abortion-A Prospective Study. *Indian J Obstet Gynecol Res* [Internet]. 2015 [cited 2021 Aug 19];2(4):227. Available from:  
<http://www.indianjournals.com/ijor.aspx?target=ijor:ijogr&volume=2&issue=4&article=004>
32. Kulkarni KK. Pre-induction with Mifepristone for Second Trimester Termination of Pregnancy. *J Obstet Gynecol India* [Internet]. 2014 Apr [cited 2021 Jun 2];64(2):102–4. Available from: <http://link.springer.com/10.1007/s13224-013-0472-5>
33. Practice Bulletin No. 135: Second-Trimester Abortion. *Obstet Gynecol* [Internet]. 2013 Jun [cited 2021 Nov 15];121(6):1394–406. Available from:  
[https://journals.lww.com/greenjournal/Fulltext/2013/06000/Practice\\_Bulletin\\_No\\_\\_135\\_\\_Second\\_Trimester.42.aspx](https://journals.lww.com/greenjournal/Fulltext/2013/06000/Practice_Bulletin_No__135__Second_Trimester.42.aspx)

34. 3270 RCOG Abortion guideline.qxd. :145.
35. Safe abortion: technical and policy guidance for health systems. *Reprod Health Matters* [Internet]. 2012 Jan [cited 2021 Aug 19];20(39):205–7. Available from: <https://www.tandfonline.com/doi/full/10.1016/S0968-8080%2812%2939623-7>
36. Nissi R, Santala M, Immonen E, Talvensaari-Mattila A. Mifepristone and misoprostol is safe and effective method in the second-trimester pregnancy termination. *Arch Gynecol Obstet* [Internet]. 2016 Dec [cited 2021 Jun 2];294(6):1243–7. Available from: <http://link.springer.com/10.1007/s00404-016-4169-8>
37. Nagaria T, Sirmor N. Misoprostol Vs Mifepristone and Misoprostol in Second Trimester Termination of Pregnancy. *J Obstet Gynecol India* [Internet]. 2011 Dec [cited 2021 Dec 7];61(6):659–62. Available from: <http://link.springer.com/10.1007/s13224-011-0118-4>
38. Patel U, Chauhan K, Singhi S, Kanani M. Second trimester abortion- mifepristone and misoprostol or misoprostol alone? *Int J Reprod Contracept Obstet Gynecol* [Internet]. 2013 [cited 2021 Aug 19];315–9. Available from: <http://www.ijrcog.org/index.php/ijrcog/article/view/100>
39. Borgatta L, Kapp N. Labor induction abortion in the second trimester. *Contraception* [Internet]. 2011 Jul [cited 2021 Aug 3];84(1):4–18. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0010782411000576>

40. Ngoc NTN, Shochet T, Raghavan S, Blum J, Nga NTB, Minh NTH, et al. Mifepristone and Misoprostol Compared With Misoprostol Alone for Second-Trimester Abortion: A Randomized Controlled Trial. *Obstet Gynecol* [Internet]. 2011 Sep [cited 2021 Aug 19];118(3):601–8. Available from: <https://journals.lww.com/00006250-201109000-00015>
41. Joensuu-Manninen H, Kuvaja P, Talvensaari-Mattila A. Clinical efficacy of mifepristone and misoprostol in second trimester pregnancy termination. *Acta Obstet Gynecol Scand* [Internet]. 2010 [cited 2021 Dec 7];89(12):1552–6. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.3109/00016349.2010.513427>
42. Mentula M, Suhonen S, Heikinheimo O. One- and two-day dosing intervals between mifepristone and misoprostol in second trimester medical termination of pregnancy--a randomized trial. *Hum Reprod* [Internet]. 2011 Oct 1 [cited 2021 Aug 3];26(10):2690–7. Available from: <https://academic.oup.com/humrep/article-lookup/doi/10.1093/humrep/der218>
43. Elami-Suzin M, Freeman MD, Porat N, Rojansky N, Laufer N, Ben-Meir A. Mifepristone Followed by Misoprostol or Oxytocin for Second-Trimester Abortion: A Randomized Controlled Trial. *Obstet Gynecol* [Internet]. 2013 Oct [cited 2021 Dec 7];122(4):815–20. Available from: [https://journals.lww.com/greenjournal/Fulltext/2013/10000/Mifepristone\\_Followed\\_by\\_Misoprostol\\_or\\_Oxytocin.13.aspx](https://journals.lww.com/greenjournal/Fulltext/2013/10000/Mifepristone_Followed_by_Misoprostol_or_Oxytocin.13.aspx)

44. Hamoda H, Ashok PW, Flett GMM, Templeton A. A randomized trial of mifepristone in combination with misoprostol administered sublingually or vaginally for medical abortion at 13–20 weeks gestation. *Hum Reprod* [Internet]. 2005 Aug 1 [cited 2021 Dec 7];20(8):2348–54. Available from:  
<http://academic.oup.com/humrep/article/20/8/2348/618559/A-randomized-trial-of-mifepristone-in-combination>
45. Hou S-P, Fang A-H, Chen Q-F, Huang Y-M, Chen O, Cheng L-N. Termination of second-trimester pregnancy by mifepristone combined with misoprostol versus intra-amniotic injection of ethacridine lactate (Rivanol®): a systematic review of Chinese trials. *Contraception* [Internet]. 2011 Sep [cited 2021 Aug 3];84(3):214–23. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0010782411000278>
46. Wildschut H, Both MI, Medema S, Thomee E, Wildhagen MF, Kapp N. Medical methods for mid-trimester termination of pregnancy. *Cochrane Fertility Regulation Group*, editor. *Cochrane Database Syst Rev* [Internet]. 2011 Jan 19 [cited 2021 Aug 3]; Available from: <https://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005216.pub2>

## APPENDICES

### PATIENT INFORMATION SHEET

Date: \_\_\_\_\_

You are being requested to participate in a study to see if a drug called Misoprostol is more effective when used alone or when used in combination with another drug called Mifepristone for termination of pregnancy from 12 weeks to 20 weeks. In our hospital, 2 regimens are being followed for medical termination of pregnancy between 12 - 20 weeks of gestation, depending on the treating doctor's preference.

**One method of termination of pregnancy is by using tablet Misoprostol alone:**

Tablet Misoprostol is administered vaginally or orally, 400 microgram every 4-6 hours for a maximum of 6 times or 800 microgram every 12 hours for a maximum of 3 times.

**Second method of termination of pregnancy is by using tablet Mifepristone along with tablet Misoprostol:** Tablet Mifepristone 200 mg orally on day 1 and on day 3, tablet Misoprostol is administered as per the dosage mentioned in method 1. This study is conducted to assess which of the two methods is more effective, safer and cheaper. We hope to include about 100 people from this hospital in this study.

**If you take part, what will you have to do?** If you agree to participate in this study, we will note your demographic details, the scan findings, diagnosis, the regimen used to terminate pregnancy, number of doses needed for complete expulsion of products of conception, side effects like fever, vomiting, diarrhea and complications like excessive bleeding, need for blood transfusion, surgical evacuation, length of hospital stay. Please note that this study is just an observational study and all the decisions with respect to your treatment will be made by your treating doctor. You will have no additional risk or benefit by participating in the study.

**Can you withdraw from this study after it starts?** Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

**Will your personal details be kept confidential?** The results of this study may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

**If you have any further questions, please contact Dr Sonia Baby John (Email: [soniababyjohn@gmail.com](mailto:soniababyjohn@gmail.com), Mobile number: 7356876265, Department of Obstetrics and Gynaecology, CMC Vellore)**

## CONSENT FORM

**Study Title:** *Comparison of efficacy of Misoprostol alone over Mifepristone and Misoprostol combination for termination of pregnancy from 12 to 20 weeks gestation: A prospective observational study.*

**Date:**

**Study Number:**

**Subject's Name:**

**Date of Birth / Age:**

**Hospital Number:**

**Phone Number:**

1. I confirm that I have read and understood the information sheet dated \_\_\_\_\_ for

the above study and have had the opportunity to ask questions. (    )

2. I understood that my participation in the study is voluntary and that I am free to withdraw

at any time, without giving any reason, without my medical care or legal rights being affected. (    )

3. I understand that the ethics committee and the regulatory authorities will not need my

permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. (    )

4. I agree not to restrict the use of any data or results that arise from this study, provided such a use is only for scientific purpose. (    )

5. I agree to take part in this study. (    )

i) Signature/ thumb impression of the subject:

Name of the subject:

Date:

ii) Signature/ thumb impression of the witness:

Name of the witness:

Address of the witness:

Date:

iii) Signature of the investigator:

Name of the investigator:

Date:



## PERFORMA

**Serial number -**

**Hospital number -**

**Name -**

**Unit - 3, 4, 5**

**Booked - Inside / outside**

**DOB** \_\_/\_\_/\_\_\_\_\_

**Age** \_\_

**Parity G** \_\_ **P** \_\_ **L** \_\_ **A** \_\_

**Previous h/o abortions: Yes/No**

1. GA - \_\_weeks \_\_days

2. CA. – Present / Absent

3. Indication: 1- VTOP, 2-MA, 3- Spont. A 4 -Others

4. Mode: 1-Spont, 2-MTP, 3-surgical evacuation, 4-(MTP + Surgical)

5. Others

**LMP:** \_\_/\_\_/\_\_\_\_\_

**Scan EDC:** \_\_/\_\_/\_\_\_\_\_

**Gestation at diagnosis:** \_\_ + \_\_

**Gestation at TOP:** \_\_ + \_\_

**DOA** \_\_/\_\_/\_\_\_\_\_

**DOD** \_\_ / \_\_ / \_\_\_\_\_

**Duration of hospital stay** \_\_ (days)

**Indication for termination:**

CNS: Yes/No

CVS: Yes/No

Renal: Yes/No

Skeletal: Yes/No

Others:

**Mifepristone:** Yes/No

If yes, Mifepristone date \_\_ / \_\_ / \_\_\_\_\_

If yes, Mifepristone time \_\_. \_\_ hours

**Misoprostol:** Yes/No

If yes, Misoprostol dose –

Misoprostol no. of doses –

Misoprostol frequency \_\_ (Hours)

Misoprostol 1st dose date \_\_ / \_\_ / \_\_

Misoprostol 1st dose time \_\_: \_\_ hours

**Re-induction:** Yes/No

Date: \_\_ / \_\_ / \_\_\_\_\_, time \_\_: \_\_ hours

Method:

**Expulsion date:** \_\_ / \_\_ / \_\_\_\_\_,

**Expulsion time:** \_\_: \_\_ hours

**Complications:** Yes/No

If yes 1. Excessive bleeding, 2. Infection, 3. RPOC, 4. Retained placenta. 5. Blood transfusion. 6. Others

**Procedure:** Yes/No

If yes 1. MVA, 2. MROP, 3. Others

**Obstetric co – morbidities:** Yes/ No

If yes, GDM, HTN, previous LSCS, Infertility, fibroid uterus, APLA, PPRM, others.

**Medical – comorbidities:** Yes/ No

If yes, diabetes, HTN, thyroid disorders, obesity, seizure disorder, asthma, heart disease, renal, autoimmune, others.

**Antibiotic usage** Yes/ No

**Bill:**

**Ward:**

**Follow up:** Yes/No

# DATA SHEET

sino	hospsno	name	unit	booked	dob	age	g	p	l	a	prevabror	ga	ca	indicat	mode	others	Imp	edcsan	gadiag	gatop	doa	dod	hosps	cms	cvb		
1	2000166	Siya Francis	3		15/04/1995	25	2	1	1	0	2							31/08/2020		19.1	19.3	13/01/2021	15/01/2021	3	1		
2	200215	GIRIJA S	3	2		24	1	0	0	0	2							29/09/2020			15.2	14/01/2021	17/01/2021	4			
3	073825	MITA DAS	5	1		26	3	2	0	0	2								17/07/2021	14.1	14.4	16/01/2021	21/01/2021	4			
4	638822	G NANASOUNDARI	5	1		28	1	0	0	0	2								30/06/2021	16.5		20/01/2021	27/01/2021	8			
5	420765	RUBEENA ANJUM	4	1		32	2	1	1	0	2										17.4	18.3	21/01/2021	22/01/2021	2		
6	524305b	lakshmi	3	1		23	1	0	0	0	2							14/09/2020									
7	775473h	sangeetha r	4	1		27	2	0	0	1	1	20.4			1	2		05/11/2020				12.5	03/02/2021	03/02/2021	1	1	
8	009544p	lavanya g	5		23/06/1995	25	1	1	1	1	1								18/07/2021		16.6	17.1	08/02/2021			1	
9	873364d	gajalaxkshmi	4	1		35	2	0	0	1	1	8						01/11/2020			13.5	13.6	08/02/2021	09/02/2021	2		
10	036205p	VIWEKHA K P	3		02/09/2021	21	1	0	0	0	2							07/10/2020		25/07/2021	16.2	16.2	09/02/2021	09/02/2021	1		
11	558604h	RAMANI S	4	1	07/01/2002	19	4	2	0	1	1	15.3	1		1	2	FOR FETU	25/10/2020	12/08/2021	14.5	15.1	08/02/2021	09/02/2021	2			
12	346004h	SILAMBARASI M			22/06/1990	30	4	2	2	1	1	15.2	1		1	2				14/11/2020		11.5	13	02/02/2021			1
13	053839p	SURYA V	4	2	13/05/1990	30	4	2	1	1	1	8	1		1	3					18.6	18.6	13/02/2021	15/02/2021	3	2	
14	049279p	TAHIYEL	5	1		27	1	0	0	0	2							06/11/2020			14.3	15.3	15/02/2021	16/02/2021	2	1	
15	202847p	SOBIKA	5	1		25	1	0	0	0	2							21/11/2020			12.2	12.2	17/02/2021	19/02/2021	3		
16	669009h	NANDHINI K	4	2		21	2	1	1	1	2							20/11/2020			12.5	12.5	17/02/2021	19/02/2021	3		
17	193450D	KALAISILUNI	4	1		34	2	1	1	0	2							25/10/2020			16.2	16.5	19/02/2021	21/02/2021	3		
18	027736p	TAMILARASI	3	1		31	1	0	0	0	2							05/11/2020			15	15.3	21/02/2021	23/02/2021	3		
19	669699f	SINDHIAL V	5	1		30	3	2	2	0	2							18/10/2020			18.6	19.1	01/03/2021	02/03/2021	2		
20	954179h	RADHIKA E	3	1		29	1	0	0	0	2							20/10/2020			18.1	19.3	04/03/2021	08/03/2021	5		
21	061485p	VAISHNAVI	5	1		26	1	0	0	0	2							22/11/2020			11	14.4	04/03/2021	05/03/2021	2		
22	033078p	ZEENATH	3	1		19	1	0	0	0	2							22/10/2020			19	19.2	04/03/2021	06/03/2021	3		
23	073486p	DHANALAKSHMI	4	1		32	1	0	0	0	2							07/12/2020			13.1	14	15/03/2021	16/03/2021	2	1	
24	346754g	bhagyalakshmi	3	1		25	2	0	0	1	1	16.2			2	3		02/11/2020			19.3	16.2	18/03/2021	20/03/2021	3	1	
25	675669h	archana	3	1		26	2	1	1	1	2								29/08/2021		16.3	16.4	19/03/2021	20/03/2021	2		
26	065661h	parvati kumari	4	1		25	1	0	0	0	2							10/12/2020			19.4		25/03/2021	27/03/2021	3		
27	939512g	thenmozhi	3	1		30	3	0	0	1	1	8	3		1			29/10/2020			19.2	19.3	26/03/2021	27/03/2021	2		
28	091485p	vanitha	5	1		23	2	0	0	1	1	30	2					10/11/2020			20	20	05/04/2021	06/04/2021	2		
29	086713p	sangeetha r	4	1		23	3	1	1	1	1	11.1			2	3		22/12/2020			13.3	15.2	08/04/2021	09/04/2021	2		
30	097055p	vanjikodi	4	1		29	1	0	0	0	2							21/12/2021			12.4	12.4	19/04/2021	20/04/2021	2		
31	262933p	sonndhariya	3	2		20	2	1	1	1	1										12.4	12.4	22/04/2021	23/04/2021	2		
32	230341p	priya m	5	1		23	1	0	0	0	2							27/11/2021			18.2	18.2	04/04/2021	14/04/2021	10		
33	262335p	preethika	3	1		27	2	0	0	1	1	11	2		3			09/01/2021			13.6	13.6	16/04/2021	18/04/2021	3		
34	099294p	benicia	5	1		26	1	0	0	0	2							06/01/2021			14.3	14.3	17/04/2021	19/04/2021	2		
35	894525g	pushpa m	4	1		29	4	1	1	0	1	12	1		2			08/12/2021			12.1	17.4	19/04/2021	20/04/2021	2		
36	678963g	sandhya	4	1		31	2	0	0	1	1	22	1		2			27/12/2020			16	16	19/04/2021	20/04/2021	2		
37	093870p	nandhini g	4	1		27	5	0	0	4	1	12.6			3	1		23/11/2020			13.3	16.4			2	1	
38	095629p	umamaheshwari j	3	1		36	1	0	0	0	2							17/01/2021			14	14.3	28/04/2021	04/05/2021	7		
39	362604h	asha m	3	1		24	4	1	1	2	1	30	3		1			01/02/2021			12.4	12.4	30/04/2021	01/05/2021	2	1	
40	099941p	borndlee	4	1		43	2	1	1	1	2							29/01/2021			14	14.2	10/05/2021	12/05/2021	3		
41	263019p	MASILA	5	1		35	4	3	3	0	2							06/10/2021			19	19	12/05/2021			1	
42	482643D	PUNITHA	3	1		30	6	3	2	0	1	6			1	2		08/01/2021			17.6	18.3	17/05/2021	18/05/2021	2	1	
43	263463p	NANCY	4	1		23	1	0	0	0	2							22/01/2021			15.4	16	14/05/2021	15/05/2021	2		
44	800273h	SASIKALA	5	1		28	4	0	0	3	1	24	3		1			17/02/2021			12.5	12.5	17/05/2021	20/05/2021	4		
45	6361491	KALARASI	4	1		35	3	2	2	0	2							26/02/2021			12.3	12.3	24/05/2021	26/05/2021	3		
46	417551h	INDHUMATHI	4	1		29	2	1	1	1	2							16/02/2021			19.4	13.5	23/05/2021	27/05/2021	5	1	
47	659910h	MADHUMITHA	5	1		26	1	0	0	0	2							01/03/2021			12	12	24/05/2021	26/05/2021	3		
48	095293h	MANIULA K	5	1		29	5	1	1	3	1	8			2	3		22/02/2021			13.3	13.3	24/05/2021	28/05/2021	5		
49	241170p	PRİYADARSHINI	4			20	2	1	1	0	2							22/01/2021			18.4	19.1	05/06/2021	06/06/2021	2	1	
50	241901p	UMA MAHESHWARI	4	1		39	2	0	0	1	1	6	3		1			03/03/2021			13.5	13.5	07/06/2021	08/06/2021	2		
51	852901D	UMA NATARAJAN	4	1		40	3	1	1	1	1	24	1		4	1		05/02/2021			12.3	12.3	30/05/2021	02/06/2021	4		
52	555651D	SUGANTHI	3	1		30	3	2	2	0	2							16/01/2021			20	20	05/06/2021	06/06/2021	2	1	
53	897671F	CHARULATHA N	3	1		23	1	0	0	0	2							14/12/2021				13	13	04/06/2021	09/06/2021	6	
54	797301G	LATHA M	3	1		35	1	0	0	0	2							18/02/2021				15.6				1	
55	245459P	SAYIRA BANU	3	2		22	2	1	1	1	1							15/02/2021				17.3	19/06/2021	20/06/2021	2		
56	924000h	PUMITHA VAVI	5	1		24	2	1	1	0	2							19/03/2021				13.3	13.3	21/06/2021	21/06/2021	3	
57	521521h	yamuna rani	4	1		25	1	0	0	0	2										12.3	12.3	31/07/2021	03/08/2021	4		
58	252940p	valarmathi k	5	1		34	2	0	0	1	1	8	3		3			09/02/2021		07/12/2021	18	18	06/07/2021	08/07/2021	3	1	
59	258446p	swetha	5	1		17	2	0	0	1	1	12	2		3			09/04/2021			14.3		19/07/2021	21/07/2021	3		
60	268149b	anisha	5	1		26	1	0	0	0	2							02/03/2021			17.3		04/07/2021	05/07/2021	2		
61	588416h	jyothi v	5	1		27	2	0	0	1	1	8	2		2			12/02/2021			15.6		05/07/2021	07/07/2021	3		
62	805756g	farheena	5	1		28	2	1	1	0	2							16/03/2021			19.5	19.5	28/06/2021	30/06/2021	3		
63	848439d	shenbagam	5	1		32	3	2	2	0	2							19/03/2021			19		27/07/2021	28/07/2021	2		
64	608289h	prabha s	5	1		29	1	0	0																		

renal	skelet	othind	mifep	mifedate	mifetme	misopr	misodose	misodone	misofreq	misodate	misotime	reinduc	reindate	reintime	reinmet	expudate	exputime	comp	compes	proced	proces	obscomor
		MA	2			1	400	4	6	13/01/2021	22	1		2400	21/01/2021	11.1	2			2		1
		MA	2			1	200	3	6	14/01/2021	20			17 600	15/01/2021	13	1	1	2			1
1			2	18/01/2021	12	1	400	1	6	20/01/2021	12.45			4.45 400	20/01/2021	17.31	2			2		1
			2			1	400	6	6	21/01/2021	2	1	25/01/2021	3200	25/01/2021	2.05	2			2		1
		arnold chiari malformation	1	19/01/2021	17	1	400	1	6	21/01/2021	16.3			5 400	21/01/2021	21.3	1	1	1	1		1
			2			1	800	3	12					33 2400	03/02/2021	4.3	1	3	1	1	1	2
			2	02/02/2021	15	2						2			03/02/2021	18	1	3	1	1	1	1
			2			1	400	2	6	08/02/2021	16.3			8.2 800	09/02/2021	0.5	2			2		2
		Hydrops and suspected AVSD	1	06/02/2021	17	1	800	1	12	08/02/2021	17.15			12.45 800	09/02/2021	6	1	1	1	1	1	2
		MA	2			1	400	1	6	09/02/2021	8			4.5 400	09/02/2021	12.5	2			2		2
		FETUS HOMOZYGOUS FOR PRO	1	06/02/2021	21	1	400	1	6	08/02/2021	21			3.4 400	09/02/2021	0.4	2			2		1
			2	11/02/2021	17	1	800	1	12	13/02/2021	12.15			2.15 800	13/02/2021	16.3	2			2		1
2	2	MA	2			1	400	1	6	13/02/2021	12			8.37 400	13/02/2021	20.37	2			2		1
			2			1	400	2	6	15/02/2021	14.3	2		33 800	16/02/2021	23.3	2			2		2
		MA	2			1	800	3	12	17/02/2021	7	2		37 2400	18/02/2021	20	1	3	1	1	1	2
		MA	2			1	800	3	12	17/02/2021	10.45	2		2400			1	1	1	1	1	2
		MA	2	16/02/2021	22	1	600	3	6	19/02/2021	17	2		29 1800	20/02/2021	22	1	3	1	1	1	1
		MCDNA TRAP	1	19/02/2021	22	1	400	3	6	21/02/2021	22	2		20 1200	22/02/2021	18	2			2		2
		ECTRODACTYLY	2			1	400	2	6	01/03/2021	18	2		10 800	02/03/2021	4	2			2		2
		HETERO TAXY	1	02/03/2021	13	1	400	3	6	04/03/2021	13	2		13 1200	05/03/2021	14	1	3	1	1	1	1
		CYSTIC HYGROMA	2			1	400	1	12	04/03/2021	12.3	2		8.5 800	04/03/2021	21.2	2			2		2
		MA	2			1	800	3	6	04/03/2021	20.45	2		24.4 1200	05/03/2021	21.25	1	3	1	1	1	2
		ARNOLD CHIARIIC II	1	13/03/2021	21.3	1	600	1	6	15/03/2021	19.15	2		6 600	16/03/2021	0.5	1	6	2			1
		2nd twin 1st twin IMD	2			1	400	2	6	18/03/2021	18			10 800	19/03/2021	4	1	4	1	2	1	2
		cystic hygroma	2			1	400	2	6	19/03/2021	16.3	2		9.1 800	20/03/2021	1.4	1	3	1	1	1	2
		MOTHER - CA RECTUM	2			1	400	2	6			2		21 1600	27/03/2021	14	2			2		2
		MA	2			1	400	3	6	26/07/2021	17.3	2		17.15 1200	27/03/2021	10.45	2			2		2
		arnold chiriic	1	03/04/2021	15.3	1	400	3	6	05/04/2021	17	2		19.5 1200	06/05/2021	12.5	2			2		1
		MA	1	06/04/2021	18	1	600	1	6	08/04/2021	19.3	2		4.15 600	08/04/2021	23.45	1	3	1	1	1	1
		MA	1	17/04/2021	18	1	800	1	12	19/04/2021	17	2		4.45 800	19/04/2021	21.45	2			2		2
		MA	2			1	800	1	12	22/04/2021	14	2		11.3 800	23/04/2021	1.3	1	1	1	1	1	2
		MA	2			1	400	6	6	04/04/2021	17.3	2		43.2 2400	06/04/2021	12.5	2			2		1
		MA	2			1	800	3	12	16/04/2021	10	2		30.3 2400	16/04/2021	16.3	1	3	1	1	1	2
		MA	2			1	800	3	12	17/04/2021	16.45	2		41.3 2400	19/04/2021	10.15	2			2		2
		hydrops t21	1			1	600	3	6			2		16 1800	20/04/2021	10	2			2		1
		MA	1			1	600	2	6			2		9 1200	20/04/2021	5	1	3	1	1	1	1
			2	15/04/2021	20	1	600	1	6			2		2.3 600	17/04/2021	18.3	1	3	1	1	1	1
		hydrops	2			1	600	3	6	28/04/2021	17.3	2		17 1800	29/04/2021	10.3	1	1	1	1	1	1
			2			1	800	1	12	30/04/2021	20.3	2		10.3 800	01/05/2021	7	2			2		2
		juvenile onset ALS type 2	1	09/05/2021	22	1	600	2	6	11/05/2021	10	2		9.3 1200	11/05/2021	19.3	2			2		1
		MATERNAL EBA	2			1	400	2	6	12/05/2021	18.45	2		7.2 800	13/05/2021	2.24	1			2		2
			2	15/05/2021	21	1	400	1	17	05/2021	15	2		3 400	17/05/2021	18	1	6	2			1
		MA	1	11/05/2021	12	2						2			13/05/2021	6	1	3	1	1	1	2
		MA	2			1	800	2	12	10/05/2021	14	2		1600			1	3	1	1	1	2
		MA	1	22/05/2021	21.3	1	800	3	12	24/05/2021	21.15	2		30 2400	26/05/2021	5.15	2			2		2
		MA	1	21/05/2021	21.3	1	600	5	6	23/05/2021	22.45	2		35.25 3000	25/05/2021	10.2	1	3	1	1	1	1
		MA	2			1	800	3	12	24/05/2021	16	2		24 2400	24/05/2021	16	2			2		2
		MA	2			1	800	3	12	25/05/2020	8.3	2		27 2400	27/05/2021	11.3	1	3	1	1	1	1
			1			1	400	2	6					4 400	05/06/2021	20.02	2			2		1
1		MULTIPLE HYDROPS	2			1	800	1	12					10.3 800	08/06/2021	4	1	3	1	1	1	2
		MA	1	28/05/2021	20	1	800	3	12	30/05/2021	11	2		6.1 2400	30/05/2021	17.1	1	3	1	1	1	1
			2			1	400	2	6	05/06/2021	16.3	2		13.45 800	05/06/2021	18.15	2			2		1
		CONJOINT TWIN WITH ACARDI	2			1	800	3	12	04/06/2021	14.15	2		2400			2			2		1
			2	09/06/2021		1	800	1	12	12/06/2021	14.15	2		8.15 800	12/06/2021	22.3	1	1	1	1	1	2
		PREVIABLE PPRM	2			1	400	1				2		6 400	19/06/2021	23	2			2		2
		MA	2			1	800	2	12	21/06/2021	12	2		22.3 1600	22/06/2021	10.3	1	1	1	1	1	2
		MA	1			1	800	2	12			1		1600			2			2		1
1			2			1	400	6	6			2		62.3 2400	08/07/2021	9.3	2			1	1	2
		1 omphdocelle	2			1	800	1	2			2		22 1600	20/01/2021	20	2			2		2
		MA	2			1	800	1				2		9.3 800	04/07/2021	2	1	3	1	1	1	2
		HEMOPHILIA	2			1						2		17 1800	06/07/2021	10	1	3	1	1	1	1
			2			1								20 1600	29/06/2021	15	2	1	1	3	2	
1			2			1		2				2		14 800	28/07/2021	10.3	1	2	2			1
		MA	2			1	800	2	12	22/06/2021	2	2		16 1600	22/06/2021	10	1	1	1	1	1	1
		MA	2			1	400	4	6					24.3 1600	23/07/2021	21.3	1	3	1	1	1	1
		MA	2			1	800	1				2		11.3 800	04/07/2021	6.3	1	1	1	1	1	2
		MA	2			1	800	2	12			2		15.3 1600	01/06/2021	7.3	2			2		2
		MA	2			1	400	4	6					29.45 1600	04/08/2021	0.45	2			2		2
		MA	2			1	400	7	6			2		48 2800	20/08/2021	20	1	3	1	1	1	2
		cystic hyproma	2			1	400	2				2		8 800	25/08/2021	5	2			2		2
			2			1	800	3	12			2		18 2400	26/08/2021	20.3	2			2		2
		MA	2			1	400		6			2		26.3 1600	15/08/2021	20.3	1	3	1	1	1	2
		MA	2			1								34 2400	12/08/2021	5	2			2		1
		trisomy 21 cystic hygrma	1			1						2		6 400	25/08/2021	14	1	3	1	1	1	2
1		ANHYDRAMNOS, DOWN'S HIG	1	10/01/2021	19.45	1	400	2	6	12/01/2021	19	2		15.3 800	13/01/2021	10.3	2			2		1
		MA	1	01/09/2021	15	1	800	2	12	03/09/2021	15	2		14.3 1600	04/09/2021	17.3	2			2		1
		MA hydropic changes cystic hy	1	01/09/2021	19	1	800	2	12	03/09/2												

obsyes	medcomor	dm	htn	thyroid	obesity	seizure	asthma	heart	renal1	autoimmu	othcomor	antibiot	bill	ward	fup
3	1	1										1			
8	2											27380			1
3	2											211383	G4N		1
4	1			1								2	G7S		1
1	1			1								26953			1
2	2											214265	G4E		2
8	2											26260	G4s		2
2	2											2			
4	2											29840			1
2	2											210995			1
8	2											24495			
8	2										PREVIOUS ANOM	214250			1
3	2										PREVIOUS END	220462			
1	1										aNEMIA	220000			
2	2											25991	G3S		
2	2											28680	G4S		
3	2											210000	G4S		
2	2											210590	G4E		
2	2											26140	G4N		
1	2										RETAINED PLACE	139867	G4E		
1	1			1							SLE	2	G7S		
2	2											115446	G4E		
8	1			1							FEVER, RHnegati	25000	G4s		
2	2										twins	224681	G4e		
2	2											210097	G4e		
1	2										low BMI CA RECT	217040	G4e		
2	2											29131	G4e		
8	2										rh negative	220000	G4n		
3	2											25800	G4s		
2	2											27225			
1	1										rov cyst	226302	G4e		
8	2											147460	G4n		
1	1			1								112145	G3s		
2	2											2	G7s		
8	2										prev GDM, Prev I	26475	G4s		
8	1	1									previous anoma	28000	G4s		
8	2										recurrent t1 loss	23500	G4s		
1	1			1							fever, prev lap n	126570	G4e		
1	1	1										24818	G4e		
8	1		1	1							PREVIOUS BABY :	2	G7S		
1	1							1			FEVER, EBA NYHA	118925	G4N		
8	2										FEVER, PREV CHII	28857	G4E		
2	2											27355	G4S		
1	1										SLE 2 ALPHA +VE	210000	G4N		
2	2											29240	G4S		
3	1										UNDER WT	215180	G4S		
2	2											2	G7S		
1	1	1		1					1		PREV HTN, PREV	220742	G4N		
3	2											28970	G4S		
1	2											13500			
8	2										PREVIOUS LSCS F	218600	G4S		
1	1										PREVIOUS IUGR	28483	G4E		
2	2										R breast fibroad	234905	G4E		
2	2											222469			
1	1							1				25375	G4E		
1	2											16175	G4n		
2	2											2	G3S		
8	2											211495			
2	2											27095	G4n		
8	2											25710	G4n		
2	2											22500	G4n		
1	1										underweight	114195			
8	2										prev anomalous	16355	G4n		
4	1							1			under weight	117020	G4n		
4	1							1				2	G3S		
2	2											216005	G4s		
2	2											210263	G3S		
2	2											29770	G4n		
2	2											119109			
2	2											25000	G4n		
2	2											27513	G3S		
2	2											212895	G4s		
3	1										anemia	215515	G4s		
2	2											26370	G4s		
3	2											213120	G4S		
8	2											26335	G4e		
8	2											25617	G4e		
2	2											26355	G4e		
8	2											214585	G4E		
1	1								1			213280	G4E		
2	2											28795	G4E		
2	2											27230	G4N		
3	1							1				142000	G4S		
2	2											26670	G4E		
6	2											211470	G4N		
2	2											215110	G4S		
2	2											28740	G4N		
7	2											119295	G4E		
1	2											25167	G3S		
2	2											26310	G3S		
2	2											26420	G4S		
3	1										AIHA	153055	G4E		
2	2											25000	G4S		
2	2											216895	G4S		
2	2											23940	G3S		
2	2											24330	G3S		
2	2											27680	G4S		
1	1										ANEMIA	28601	G4E		
8	1										ANEMIA	224890	G4E		
2	2											211945	G4E		

