ORIGINAL ARTICLE

Association of Obstetrical Variables with Induction to Expulsion Interval in Misoprostol-Induced Mid-Trimester Abortion

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ABSTRACT:

Objective: To investigate significance association of obstetric history (maternal age, gravidity, parity, gestational age & previous LSCS) with induction to expulsion interval (IEI) in Misoprostol-induced- Mid-Trimester (MI-MT) abortion cases.

Methodology: This prospective cohort study was conducted at CMH Nowshera from January 2014- June 2015. One hundred and six candidates were included. Termination of pregnancy was carried out with Misoprostol using two regimens. Regimen A included 400ug Misoprostol given 6 hourly with maximum of 4 doses for 24 hours for gestational age 13-20 weeks. In Regimen B 200ug Misoprostol with the same protocol was given for gestational age 21-26 weeks. Failure of induction was considered after 72 hours. Cohort was stratified according to categorical variables of maternal age, parity, gravidity, gestational age and previous LSCS. Outcome variable was Induction to expulsion interval (IEI).

Results: Null hypothesis (H_0) of no significant association between obstetrical variables (maternal age, parity, gravidity, gestational age, previous LSCS) and outcome variable (IEI) was tested using chi square and Fisher's exact tests with 1000 bootstrapping. Simpson's paradox effect was adjusted using Restriction method.

Significant associations were found between gravidity, gestational age and previous LSCS with IEI (P value <0.05), that is, lower gravidity; higher gestational age and presence of previous LSCS were associated with longer IEI.

Conclusion: This study emphasized the significance of obstetric history in MI-MT abortion cases. It also emphasized important obstetrical parameters to consider hence provide guidance to clinicians and researchers for counseling, antenatal care and treatment in such cases.

Keywords: Misoprostol-induced Mid-trimester (MI-MT) abortion, Obstetric history, Induction to expulsion interval

INTRODUCTION:

There are around 30-35% of 205 million pregnancies worldwide that remain unintended. Out of which 15 to 20% end in induced abortion.[1,2] Indications most commonly described for termination of pregnancy are missed miscarriage, intrauterine fetal demise and fetal anomalies. Less common indications are preterm premature rupture of membrane (PPROM) and severe oligohydramnios.[3] Ultrasound has contributed in early recognition of conditions like fetal anomalies and fetal demise resulting in increased number of patients reporting in second trimester for termination of pregnancy.[3] Second trimester also called mid trimester is taken from 13 to 28 weeks of gestation. Around 10 to 15% of total induced abortions happen in mid trimester. With the increasing incidence of LSCS and associated complications, termination of pregnancy for some valid reasons, such as fetal abnormalities, has also increased.[4] It is a great challenge for obstetricians to deal with such patients. The most appropriate method for induced abortion is still debatable. Both medical and surgical methods have been suggested for induced abortion.[5] Medical method is preferable to surgical technique because of lower maternal morbidity and mortality, cost effectiveness and short hospital stay.[6] During the last two decades, prostaglandins are used for induction of labour, both E1 and E2 analogues.[7] Misoprostol, a synthetic E1 analogue is typically used to prevent and as a cure for peptic ulcer. Guidelines are available regarding use of Misoprostol in obstetrics and gynaecology.[8]

In low resource settings like ours, off label use of Misoprostol has been reported specially for termination of pregnancy at various gestational age, cervical ripening and labour induction in term pregnancy and also for prevention of postpartum haemorrhage.[9,10] Misoprostol can be given orally, sublingually, vaginally or rectally.[11] The routes of administration vary with the patients' compliance and the doctors' experience.[12] Side effects like diarrhea, fever and shivering are not uncommon. Sometimes at term pregnancies, misoprostol may cause uterine hyper-stimulation, CTG changes, foetal bradycardia and foetal demise.[13]

Obstetrical history of the patients plays a vital role in decision making in cases of induced abortions. There are many factors which can influence the outcome of the method used for induced abortion like maternal age, parity, gravidity, gestational age, and history of previous LSCS. Dose regimen also contributes to influence the outcome.[14] Researchers have also focused on outcome in terms of induction to expulsion interval.[15] Knowledge about induction to expulsion interval and factors influencing the time needs to be studied more as enough research has not been done on this issue.[16] This study is focused to explore the relationship between parity, gestational age and induction to expulsion time.

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METHODOLOGY:

This prospective cohort study was conducted after approval from ethical committee of the hospital. Patients with intra uterine death (IUD), foetal anomalies, and missed abortion with unknown causes who were in mid-trimester were included in the study. Abortions earlier than 13 weeks and later than 26 weeks of gestation were excluded.

The cohort was given Misoprostol orally according to gestational age as prescribed in the medical literature. Regimen A included 400ug Misoprostol given 6 hourly with maximum of 4 doses for 24 hours for gestational age 13-20 weeks, in Regimen B 200ug Misoprostol with the same protocol for gestational age 21-26 weeks. Time from induction of abortion to complete expulsion of product of conception was taken as induction to expulsion interval (IEI). Induction was considered failed after 72 hours.The cohort of misoprostol-induced mid-trimester MI-MT abortion cases was investigated for significant association of obstetric history of the patient with IEI. Five variables were taken from patient's obstetric history. These variables were maternal age, gravidity, parity, gestational age and previous LSCS. Each of these variables was taken as categorical variable that means each of them was divided into categories as shown in Figure-1. Each variable was tested against the null hypothesis of no significant association H_0 using non-parametric chi square, likelihood ratio and Fisher exact tests. For all the three tests 1000 boot strappings were performed. Each categorical variable shown in Figure-1 was tested for Simpson paradox effect.

Simpson paradox effect is a phenomenon in which the effect of a variable (association of obstetrical variables) with another variable (IEI) is reversed when a sub-category within a categorical variable (obstetrical variable here) is tested. For this purpose, gravidity was sub categorized into groups G1= Gravidity of 2 and 3, G2= Gravidity of 4 and 5 (Table-1). Other obstetrical variables were also sub categorized but none of them showed Simpson paradox effect.

Table-1
Cross tabulation of sub categories G1 and G2 of Gravidity of patients with Induction expulsion interval IEI showing the number of patients in each sub category

Gravidity of patient * Induction Expulsion Interval (IEI) Cross tabulation						
	Induction Expulsion Interval (IEI)					
Sub categories of Gravidity	< 12 HRS	12-24 HRS	24-48 HRS	48-72 HRS	FAILED INDUCTION	Total
G1	27	33	4	2	3	69
G2	16	14	3	2	2	37
Total	43	47	7	4	5	106

Figure: 1
A total of 106 Misoprostol-induced mid-trimester (MI-MT) abortion cases were taken as cohort (n=106). Number of patients shown for each obstetrical variable

Gestational Age	
13 – 20 weeks	86
21 – 26 weeks	20
Maternal Age (Years)	
15 -20	16
21 -30	80
31 -40	10
Parity	
0	6
1	36
2	44
3	18
4	2
Gravidity	
2	30
3	39
4	24
5	13

RESULTS:

Each of the categorical variables extracted from the patients' obstetric history was cross tabulated with IEI. However, none of the failed induction cases happened in gravida 2. Majority of failed induction happened in gravida 3 cases. Few cases of failed induction were also seen in gravida 4 and 5 (Figure-2).

Cross tabulation of gestational age with IEI showed that more than 80% of IEI of less than 12 hours belonged to early mid-term abortion, that is, 13-20 weeks (Table-1). In contrast, more than 80% of failed abortion cases belonged to late mid-term abortion. Figure-3 showed a very interesting staircase pattern of IEI in opposite directions for the early 13-20 week and late 21-28 week abortions. Figure-4 showed a relatively higher proportion (60%) of total cases of failed abortion occurred in patients with history of previous LSCS.

All the categorical variables were tested for their significant association with IEI using Chi square, Fisher exact and likelihood tests. Three categorical variables were significantly associated with IEI. These included gravidity, gestational age and history of previous LSCS (Table-2 – Table-4). Other categorical variables like maternal age and parity were not significant in determining IEI. Gravidity (number of pregnancies) was found important associating factor compared to parity (number of live births); although the two variables were found significantly correlated (P value <0.05).

Figure: 2

Bar chart showing the number of patients within each subcategory of Gravidity. Colour of bars shows the Induction Expulsion Interval (IEI) for each subcategory Gravida=2-5

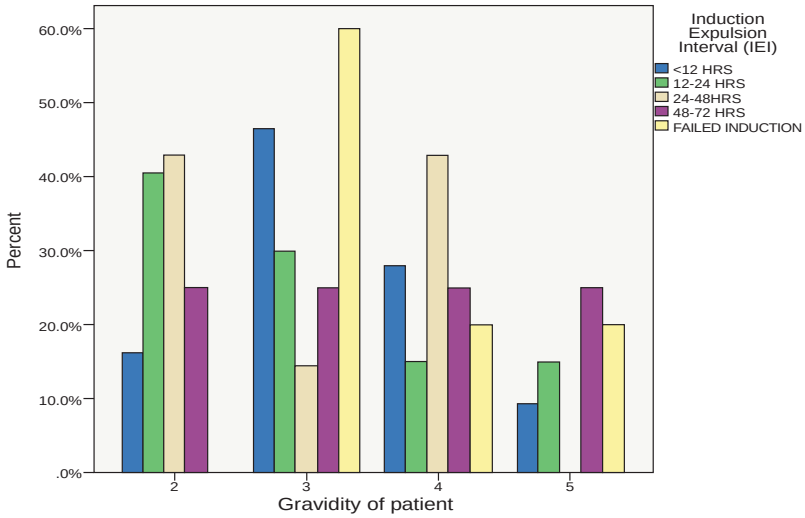

Figure: 3

Bar chart showing percentage of patients in each subcategory of gestational age. Colour of bars shows IEI for each subcategory, Gestational age: 13-20 week and 21-26 week

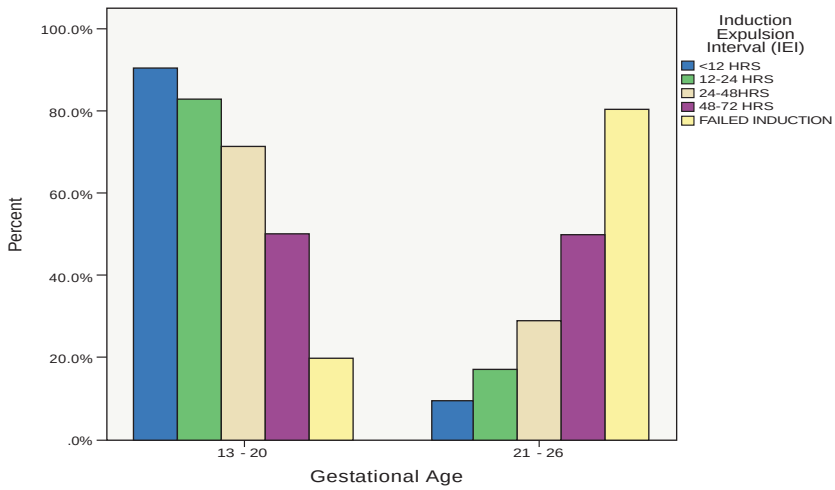

Figure: 4
Bar chart showing percentage of patients with and without history of Previous LSCS. Colour of the bars shows IEI for each subcategory: History of previous LSCS=Yes or No

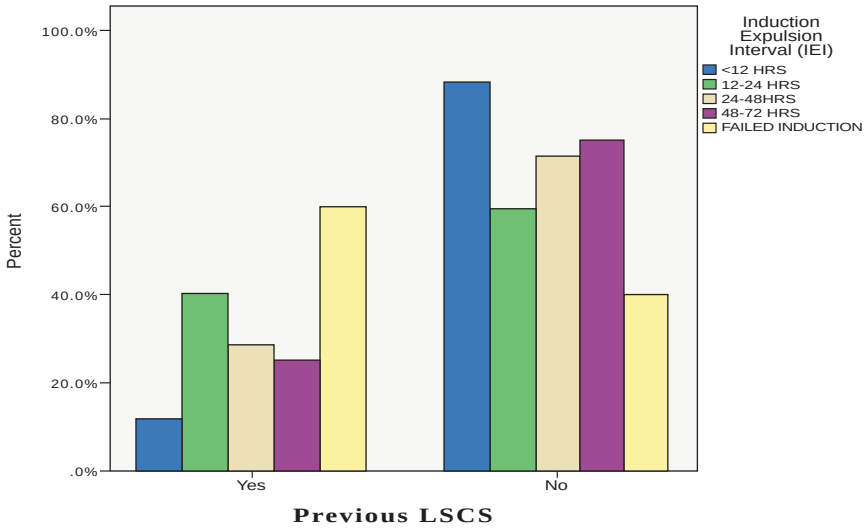

Table-2
Significant relationship of Gravidity of patient (only subcategory with Gravidity <= 3) with Induction to Expulsion Interval (IEI). Other subcategories (described in Methodology) did not show significant relationship with IEI

	Value	Degree of freedom	Asymptotic P value (2-sided)	Exact P value. (2-sided)
Pearson Chi-Square	10.013	4	0.040	0.023
Likelihood Ratio	11.315	4	0.023	0.039
Fisher's Exact Test	9.728			0.018
Linear-by-Linear Association	0.051	1	0.822	0.835
N of Valid Cases	69			

Table-3
Significant relationship of Gestational age with Induction to Expulsion Interval (IEI)

	Value	Degree of freedom	Asymptotic P value (2-sided)	Exact P value. (2-sided)
Pearson Chi-Square	17.845	4	0.001	0.002
Likelihood Ratio	14.247	4	0.007	0.006
Fisher's Exact Test	14.834			0.002
Linear-by-Linear Association	16.940	1	0.000	0.000
N of Valid Cases	106			

Table-4
Significant relationship of History of previous LSCS with IEI

	Value	Degree of freedom	Asymptotic P value (2-sided)	Exact P value. (2-sided)
Pearson Chi-Square	11.793	4	0.019	0.017
Likelihood Ratio	12.367	4	0.015	0.019
Fisher's Exact Test	12.364			0.008
N of Valid Cases	106			

DISCUSSION:

This study was aimed to investigate the significance of patient's obstetric history in estimating the induction to expulsion interval (IEI) in Misoprostol-induced mid-trimester (MI-MT) abortion cases. Results suggest that three of the obstetrical variables namely gravidity, gestational age and previous LSCS showed significant association (P value<0.05) with induction to expulsion interval (IEI). Reliability of the results was enhanced by the use of multiple statistical tests and 1000 boot strappings.

Mid trimester abortions constitute 10-15% of all induced abortions. Decision to perform the induction is made by evaluating factors that are associated with the risks and complications of the procedure. Studies suggest that the procedure of induction is more risky and complicated in cases of late gestational age as well as multiparity.[17, 18] Scioscia et al. 2007[19] reported only parity as a significant associating factor with IEI. His study was based on 423 cases of mid trimester abortion. Results have shown an association of higher parity with longer duration of IEI and early gestational age with shorter IEI.[17] Another study[20] studied 956 cases and found an association of parity and early gestational age with shorter duration of IEI. However, there are some studies that showed no significant association of parity, gravidity or gestational age with outcome of mid-trimester Misoprostol induced abortion.[21]

In the present study, the association of gravidity, gestational age and history of previous LSCS with IEI were found significant. It is worth mentioning that instead of parity which was described in the literature mentioned above as an important factor associated with outcome of Misoprostol mid trimester abortion; gravidity was found significantly associated with IEI. However, these two obstetrical variables: parity and gravidity were found significantly correlated with each other showing P-value <0.05. Although multi-gravidity has been described as a risk factor for abortion, very few studies were found that reported its effect on IEI. In this way, this study reported an interesting finding about the associating factors of IEI.

While performing the statistical analyses for significant associations of categorical variables paradoxical calculations must be kept in mind.[22] In fact, Simpson paradox is a classic example of confounding that may mask the true relationship of the two variables. Studies have suggested randomization and restriction method to overcome this problem.[23] In this study, restriction methods were used to sub categorize each categorical variable except previous LSCS. However, each sub category of three categorical variables namely gestational age, parity, and maternal age did not show paradoxical association. Only gravidity sub categories G1 and G2 showed Simpson paradoxical effect. Therefore, it is recommended that the categorical variables used for association studies in MI-MT abortion cases must be sub categorized to avoid paradoxical conclusions.

Limitations of the Study:

In this study two dose regimens for Misoprostol were used. Cohort was divided into sub-cohorts A and B on the basis of these two regimens. These two regimens were given according to gestational age of the patient. Therefore, the effects of the two regimens were addressed by categorizing gestational age according to the regimens used. However, these two regimens might have confounding effect on other categorical variables. It might be useful to study the effect of confounding variable on each categorical variable of obstetric history. However, a smaller sample size may be a limiting factor for further analyses. A larger sample size would be required to analyze the two sub cohorts separately. Studies have suggested shorter IEI with early gestational age and high parity.[24] However, results may vary due to socio-demographic factors.[25] Therefore, it is mandatory to consider the obstetrical parameters which may differ among the cohorts of different settings. Moreover, Misoprostol must be given with caution in cases of previous LSCS. Uterus rupture and need for surgical evacuation have been reported in different studies.

CONCLUSION:

This study emphasizes the importance of obstetrical history in determining the outcome of the Misoprostol induced mid trimester (MI-MT) abortion. Three of the variables namely gestational age, gravidity and previous LSCS showed significant result. Percentage distribution of number of cases in each of the three variables showed that lower gravidity, higher gestational age and presence of previous LSCS are associated with longer IEI. However, it is not justified to conclude that other variables like maternal age and parity did not influence the outcome of induced abortion. A larger sample size and a more comprehensive study design may reveal other factors associated with outcome of MI-MT abortions.

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