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ROLE OF VAGINAL MISOPROSTOL IN FAVOURABLE AND UNFAVOURABLE CERVIX IN PREGNANCY INDUCED HYPERTENSION

Original Research

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ABSTRACT

Background: Pregnancy-induced hypertension (PIH), including preeclampsia and eclampsia, remains a significant contributor to maternal and neonatal morbidity. Timely induction of labor in these patients is crucial for improving outcomes. Misoprostol, a synthetic prostaglandin E1 analogue, is gaining recognition as a cost-effective alternative to prostaglandin E2 (Dinoprostone) for cervical ripening and labor induction. Its stability at room temperature and multiple routes of administration make it particularly suitable for low-resource settings.

Objective: To determine the efficacy of vaginal misoprostol in achieving vaginal delivery among women with pregnancy-induced hypertension, comparing outcomes between those with favorable and unfavorable cervix.

Methods: This quasi-experimental study was conducted at the Department of Gynecology, Khyber Teaching Hospital, Peshawar, from July 1st to December 31st, 2024. A total of 113 women aged 20–40 years, with gestational age over 24 weeks and diagnosed with PIH, were enrolled using non-probability consecutive sampling. Vaginal misoprostol was administered every six hours in doses of 25 micrograms, up to four doses, for labor induction. Patients were continuously monitored, and successful vaginal delivery was documented as the primary outcome. Data were analyzed using SPSS version 26, with chi-square and Fisher's exact test applied at a 5% significance level.

Results: The mean age of participants was 30.50 ± 5.38 years, and the mean BMI was 23.88 ± 2.51 kg/m². Most participants were over 30 years (53.1%) and had parity ≤3 (52.2%). Of 113 patients, 85 (75.2%) had a favorable cervix and 88 (77.9%) had preeclampsia. Successful vaginal delivery occurred in 68 patients (60.2%). A significant association was found between cervical favorability and successful delivery ($p = 0.009$), while the association between PIH type and delivery outcome was not significant ($p = 0.365$).

Conclusion: Vaginal misoprostol proved effective in inducing labor, particularly among women with favorable cervical status, supporting its broader use in managing hypertensive pregnancies.

Keywords: Cervical Ripening, Efficacy, Induced Labor, Misoprostol, Pregnancy-Induced Hypertension, Preeclampsia, Vaginal Delivery.

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INTRODUCTION

Induction of labor is a commonly employed obstetric intervention aimed at initiating uterine contractions to achieve vaginal delivery within a clinically appropriate timeframe, typically between 24 to 48 hours, in women who are not yet in spontaneous labor. One of the primary strategies for labor induction involves cervical ripening, a process that uses pharmacological or mechanical means to soften, efface, and dilate the cervix, thereby improving the likelihood of successful vaginal delivery (1). Among the physical parameters assessed to determine cervical readiness are cervical length, consistency, and degree of dilation, with cervical softening being the most reliable indicator of effective induction (2). Biochemically, this softening is attributed to alterations in the collagen framework and an increase in water and amino acid content within the extracellular matrix (3). Cervical changes begin subtly early in pregnancy, even in the first trimester, and progress gradually as gestation advances. While cervical softening and effacement evolve steadily, true cervical dilatation generally commences with the onset of labor contractions and intensifies during active labor (4,5). Attempting to induce labor in the presence of an unripe cervix can be both challenging and less effective, necessitating the use of cervical ripening agents prior to or in conjunction with labor induction. Among the available methods for cervical ripening are pharmacological agents such as prostaglandins and mechanical tools like balloon catheters (6). Prostaglandin analogues, including misoprostol (E1) and dinoprostone (E2), are widely utilized in clinical practice. Misoprostol, initially developed to treat gastric ulcers, has since been repurposed due to its uterotonic properties and has shown promise in various obstetric applications such as induction of labor, management of intrauterine fetal demise, and early pregnancy loss (7). Despite prostaglandin E2's established role in cervical softening, its higher cost and refrigeration requirements have limited its widespread availability, especially in resource-constrained settings. In contrast, misoprostol offers distinct advantages, including lower cost, heat stability, diverse routes of administration, and potentially superior efficacy (8).

Notably, in one clinical trial, intravaginal administration of misoprostol—four doses of 50 micrograms administered at six-hour intervals—yielded a vaginal delivery rate of 75% in women with an unfavorable Bishop score (≤3) and 95% in those with favorable cervical status (>3), underscoring its effectiveness as a labor-inducing agent (9). However, while misoprostol has been approved for pregnancy termination in many countries, its use for labor induction, particularly in hypertensive pregnancies, remains less well explored. Preeclampsia and eclampsia continue to contribute significantly to maternal and perinatal morbidity and mortality, particularly in low- and middle-income countries (10). In such high-risk pregnancies, timely and safe induction of labor is crucial. Yet, there exists a paucity of research evaluating the efficacy of vaginal misoprostol in these populations, especially when stratified by cervical favorability. Given misoprostol's favorable pharmacological profile and accessibility, its potential as a standard induction agent in hypertensive pregnancies warrants further investigation. The objective of this study was to evaluate the effectiveness of vaginal misoprostol for labor induction in pregnant women with preeclampsia and eclampsia, comparing outcomes between those with favorable and unfavorable cervices, thereby contributing evidence toward a cost-effective and accessible alternative for cervical ripening and labor induction in high-risk obstetric populations.

METHODS

This quasi-experimental study was conducted in the Department of Obstetrics and Gynecology at Khyber Teaching Hospital (KTH), Peshawar, over a six-month period from July 1st to December 31st, 2024. A total of 113 pregnant women aged 15 to 40 years, with a gestational age greater than 26 weeks and a diagnosis of pregnancy-induced hypertension (PIH) — including preeclampsia or eclampsia — were enrolled using a non-probability consecutive sampling technique. The sample size was determined using the WHO sample size calculator, based on a 95% confidence interval, 8% absolute precision, and an expected frequency of 75% vaginal delivery in women with an unfavorable cervix following vaginal misoprostol administration (9). Preeclampsia was defined as a blood pressure reading ≥140/90 mmHg accompanied by proteinuria, while eclampsia was diagnosed in patients with preeclampsia who also experienced convulsions or other neurological manifestations. Women with known fetal distress, malpresentation on ultrasound, uterine anomalies, or a prior history of cesarean section were excluded from the study to minimize confounding risks. Cervical assessment was performed using the Bishop scoring system; a score >3 was considered favorable, while a score ≤3 indicated an unfavorable cervix. Informed written consent was obtained from all participants after explaining the purpose and procedures of the study. The research was approved by the Hospital Research Committee and the College of Physicians and Surgeons Pakistan (CPSP). Upon hospital admission, patients

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were managed under the direct supervision of a consultant obstetrician. Baseline demographics and clinical characteristics were recorded.

The intervention included the administration of 25 micrograms of misoprostol intravaginally in the posterior fornix using a sterile syringe every six hours, with a maximum of four doses permitted. Patients were closely monitored throughout for uterine activity, maternal blood pressure, and fetal heart rate by the on-duty obstetrical team. A vaginal delivery occurring within 24 hours of the initiation of misoprostol was considered a successful outcome. In cases where labor failed to progress, a cesarean section was performed. Labor prolongation was operationally defined as failure to enter or progress through the active phase of labor (defined as cervical dilatation ≥4 cm with regular uterine contractions) after 12 hours of induction or failure to achieve a cervical dilatation rate of at least 1 cm per hour once in active labor, in the absence of contraindications to vaginal delivery. This definition was used to ensure clinical consistency and reproducibility of decision-making for cesarean intervention. Data were entered and analyzed using SPSS version 22.0. Quantitative variables such as age, parity, and gestational age were summarized using mean ± standard deviation or median with interquartile range (IQR), depending on the data distribution assessed via the Shapiro–Wilk test. Categorical variables, including type of cervix, type of PIH, education, residence, socioeconomic status, and successful vaginal delivery, were expressed as frequencies and percentages. The efficacy of misoprostol in inducing vaginal delivery was compared across groups using the chi-square test; Fisher's exact test was applied where expected cell frequencies were ≤5. Potential confounding factors were addressed by stratifying the data according to relevant variables, followed by post-stratification analysis using the same statistical tests, with a p-value of <0.05 considered statistically significant.

RESULTS

The mean age of the study participants was 30.50 ± 5.38 years, with the majority (53.1%, n = 60) aged over 30 years. The mean body mass index (BMI) was calculated at 23.88 ± 2.51 kg/m². More than half of the participants (52.2%, n = 59) had a parity of three or less, and 66.4% (n = 75) were housewives. Regarding educational status, 52.2% (n = 59) had attained education above matric level, while the remaining 47.8% (n = 54) had matric or lower educational attainment. At the time of induction, 75.2% of the women (n = 85) had a favorable cervix, while 24.8% (n = 28) had an unfavorable cervix based on Bishop scoring. Preeclampsia was the predominant hypertensive disorder observed in 77.9% of patients (n = 88), while 22.1% (n = 25) were diagnosed with eclampsia. Successful vaginal delivery within 24 hours of misoprostol administration was achieved in 60.2% of participants (n = 68), while 39.8% (n = 45) required cesarean delivery due to failed progression of labor. A statistically significant association was found between cervical status and vaginal delivery success (p = 0.009). Among women with a favorable cervix, 67.1% achieved vaginal delivery, compared to only 39.3% in those with an unfavorable cervix. However, no significant association was observed between the type of pregnancy-induced hypertension and vaginal delivery outcome (p = 0.365). Among eclamptic patients, 68% (n = 17) had a successful vaginal birth, compared to 58% (n = 51) in preeclamptic patients. A detailed subgroup analysis revealed further insights into the factors influencing the efficacy of vaginal misoprostol for induction of labor. Among participants with gestational age >37 weeks, 77.8% (n = 28/36) achieved successful vaginal delivery, compared to 67.6% (n = 25/37) in those between 33–37 weeks and 60.0% (n = 15/25) in the 27–32 weeks group, suggesting a trend of increasing efficacy with advancing gestational age. With regard to parity, women with parity ≤3 showed a slightly higher rate of successful induction at 66.1% (n = 39/59) compared to 74.4% (n = 29/39) in those with higher parity. Additionally, the number of misoprostol doses administered was associated with outcome; 3–4 dose recipients had a higher rate of successful vaginal birth (n = 38/71, 53.5%) compared to those requiring only 1–2 doses (n = 30/42, 71.4%), which may indicate a selection bias wherein more responsive cases required fewer doses.

Table 1: Baseline demographics and clinical characteristics of study participants (n = 113)

Baseline characteristics		Frequency	Percent
Age (years)	30 or below	53	46.9
	More than 30	60	53.1
Parity	3 or below	59	52.2
	More than 3	54	47.8
Education	Matric or below	54	47.8
	Above matric	59	52.2
Profession	Employed	38	33.6
	House wife	75	66.4

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Table 2: Study participants according to outcome variables (n = 113)

		Frequency	Percent
Cervix status	Unfavourable	28	24.8
	Favourable	85	75.2
PIH type	Eclamsia	25	22.1
	Pre-eclmapsia	88	77.9
Efficacy (successful vaginal delivery)	No	45	39.8
	Yes	68	60.2

Table 3: Comparison of efficacy with respect to cervix status and PIH type (n = 113)

		Efficacy		Total	Chi square p value
		No (n = 45)	Yes (n = 68)		
Cervix status	Unfavourable	17	11	28	0.009
		60.7%	39.3%	100.0%	
	Favourable	28	57	85	
		32.9%	67.1%	100.0%	
PIH Type	Eclamsia	8	17	25	0.365
		32.0%	68.0%	100.0%	
	Pre-eclmapsia	37	51	88	
		42.0%	58.0%	100.0%	

Table 4: Breakdown of Gestational Age, Dosage Intervals, and Parity in Relation to Efficacy

Category	Successful Vaginal Delivery	Unsuccessful Vaginal Delivery	Total
Gestational Age 27-32 weeks	15	10	25
Gestational Age 33-37 weeks	25	12	37
Gestational Age >37 weeks	28	8	36
Parity ≤ 3	39	20	59
Parity >3	29	10	39
1-2 Doses	30	12	42
3-4 Doses	38	33	71

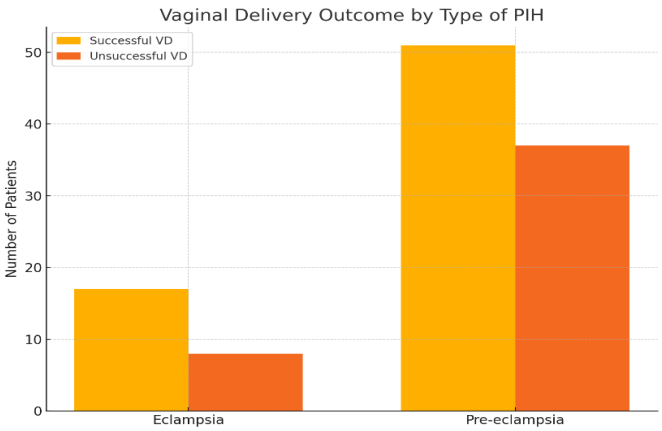

Figure 1 Vaginal Delivery Outcome by Type of PIH

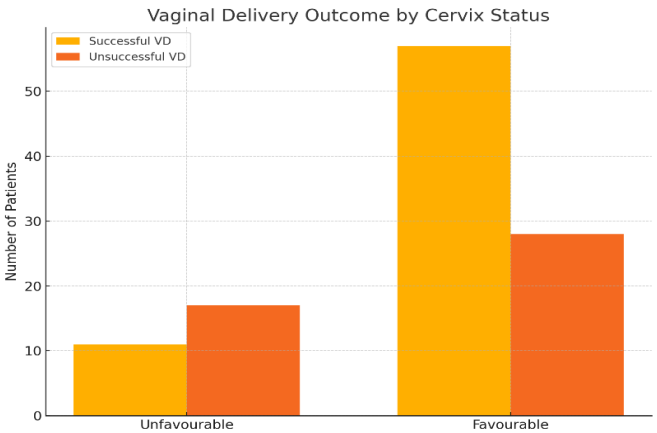

Figure 2 Vaginal Delivery Outcome by Cervix Status

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DISCUSSION

The findings of this study demonstrated that vaginal misoprostol was effective in inducing labor among women with pregnancy-induced hypertension, with a majority (60.2%) achieving successful vaginal delivery. Notably, the likelihood of successful labor induction was significantly higher in patients with a favorable cervix, emphasizing the role of pre-induction cervical status as a strong predictor of vaginal birth. This aligns with existing literature, which has established a direct relationship between Bishop score and induction outcomes, as favorable cervical conditions enhance responsiveness to induction agents (11,12). While the association between cervical status and delivery success was statistically significant ($p = 0.009$), no significant association was found between the type of hypertensive disorder and induction efficacy ($p = 0.365$). This suggests that misoprostol may exert comparable effectiveness in both preeclampsia and eclampsia when appropriately monitored. Previous studies have shown similar results, where vaginal misoprostol has been reported to induce labor effectively with minimal adverse maternal or neonatal outcomes and comparable efficacy to oxytocin, particularly in hypertensive pregnancies (13-15). A breakdown of secondary outcome trends revealed that patients with advancing gestational age showed progressively higher rates of vaginal delivery, suggesting gestational maturity may contribute to the success of labor induction. Additionally, parity played a contributory role, with multiparous women demonstrating better outcomes, consistent with existing evidence that multiparity favors vaginal delivery post-induction (16,17). Mode of birth stratified by parity in previous literature similarly highlights reduced cesarean rates among multigravida women following induction, an observation mirrored in this study. Furthermore, patients requiring fewer doses of misoprostol were more likely to have a successful vaginal birth, potentially reflecting inherent cervical favorability or heightened drug responsiveness (18,19).

However, it is important to recognize that despite the encouraging outcomes, this study had several limitations. The absence of detailed maternal and neonatal safety profiles, such as APGAR scores, uterine hyperstimulation, postpartum hemorrhage, and neonatal ICU admissions, limits the capacity to fully evaluate misoprostol's risk-benefit profile. The exclusion of induction-to-delivery interval data also restricts insight into the timeline efficiency of misoprostol in this population. Future studies should incorporate these parameters to enable more comprehensive clinical decision-making. The strengths of the study include its real-world clinical setting, inclusion of both favorable and unfavorable cervix groups, and focus on a high-risk obstetric population often underrepresented in research. The use of misoprostol in a low-resource environment further underscores its practical benefits, including cost-effectiveness and room-temperature stability compared to prostaglandin E2, making it a viable alternative in such contexts (20,21). Nonetheless, improvements in data collection concerning induction timing, safety outcomes, and patient satisfaction could enhance the applicability of findings. In conclusion, vaginal misoprostol was shown to be a clinically effective method for inducing labor in hypertensive pregnancies, with better outcomes associated with favorable cervix, advanced gestational age, and higher parity. While the findings align with existing literature, expanded research encompassing safety endpoints and standardized induction protocols is warranted to strengthen the evidence base for routine use of misoprostol in pregnancy-induced hypertension.

CONCLUSION

In conclusion, this study reinforces the clinical value of vaginal misoprostol as an effective and practical method for inducing labor in women with pregnancy-induced hypertension. Its use was associated with improved chances of vaginal delivery, particularly in those with favorable cervical conditions, while avoiding significant maternal or fetal complications. The findings support the integration of misoprostol into standard obstetric practice, especially in resource-limited settings, where its affordability, stability, and ease of administration offer considerable advantages over conventional agents. By reducing reliance on cesarean sections and promoting safer, timely vaginal births, misoprostol presents a promising option in the management of hypertensive pregnancies.

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AUTHOR CONTRIBUTION

Author	Contribution
Rabia Basri	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Fauzia Afridi*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sundas Gul	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Sadia Latif	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Dure Nayab	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Nur Taimur	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Roshni Mumtaz	Contributed to study concept and Data collection Has given Final Approval of the version to be published

REFERENCES

1. Anjali, Jain S, Pasrija S, Kille HC. Labor induction with combined low-dose oral misoprostol and Foley catheter vs oral misoprostol alone at term gestation-a randomized study. AJOG Glob Rep. 2022;2(3):100060.
2. Butler DC, Presnell SE, Bruner E, Page T, Cuff R, Phillips A. Microcrystalline Cellulose and Crospovidone Identified in Placentas With Vaginal Misoprostol Use. Am J Forensic Med Pathol. 2020;41(3):176-81.
3. de Oliveira Filgueira GC, de Fátima Pinto Rodrigues G, Benzi JRL, Nardotto GHB, Marques MP, Lanchote VL, et al. Determination of misoprostol acid in plasma samples by UPLC-MS/MS with application in a maternal-fetal pharmacokinetic study following a low misoprostol dose vaginally to induce labor. J Pharm Biomed Anal. 2021;202:114138.
4. Gomez HB, Hoffman MK, Caplan R, Ruhstaller K, Young MHH, Sciscione AC. Buccal vs vaginal misoprostol combined with Foley catheter for cervical ripening at term (the BEGIN trial): a randomized controlled trial. Am J Obstet Gynecol. 2021;224(5):524.e1-.e8.
5. Hashemi H, Hasanpoor-Azghady SB, Farahani M, Amiri-Farahani L. Comparison of the effect of vaginal misoprostol and evening primrose oil capsule with misoprostol alone on the consequences of abortion in women with intrauterine fetal death: a randomized clinical trial. BMC Complement Med Ther. 2023;23(1):248.
6. Rath W, Stelzl P, Kehl S. Outpatient Induction of Labor - Are Balloon Catheters an Appropriate Method? Geburtshilfe Frauenheilkd. 2021;81(1):70-80.
7. Sanchez-Ramos L, Levine LD, Sciscione AC, Mozurkewich EL, Ramsey PS, Adair CD, et al. Methods for the induction of labor: efficacy and safety. Am J Obstet Gynecol. 2024;230(3s):S669-s95.
8. Shahraki AD, Mirhoseini S, Movahedi M, Hajihashemy M, Haghollahi F. Comparative Study of the Effect of Vaginal use of Primrose Oil with Misoprostol on Cervical Preparation of Prim Gravid Women: A Double-blind Clinical Trial. Adv Biomed Res. 2023;12:78.
9. Sire F, Ponthier L, Eyraud JL, Catalan C, Aubard Y, Coste Mazeau P. Comparative study of dinoprostone and misoprostol for induction of labor in patients with premature rupture of membranes after 35 weeks. Sci Rep. 2022;12(1):14996.
10. Soni S, Pappas K, Lesser ML, Blitz MJ, Augustine SA, Rochelson B. Is vaginal misoprostol more effective than oral misoprostol for cervical ripening in obese women? J Matern Fetal Neonatal Med. 2020;33(20):3476-83.
11. Souizi B, Akrami R, Borzoee F, Sahebkar M. Comparison of the efficacy of sublingual, oral, and vaginal administration of misoprostol in the medical treatment of missed abortion during first trimester of pregnancy: A randomized clinical trial study. J Res Med Sci. 2020;25:72.

12. Tian S, Wang L, Han YW, Liu YN, Li FQ, Jin XH. Efficacy and safety of oral and vaginal administration of misoprostol for induction of labor in high-risk obese pregnant women with hypertension or diabetes mellitus. J Matern Fetal Neonatal Med. 2024;37(1):2327573.
13. Vorontsova Y, Haas DM, Flannery K, Masters AR, Silva LL, Pierson RC, et al. Pharmacokinetics of vaginal versus buccal misoprostol for labor induction at term. Clin Transl Sci. 2022;15(8):1937-45.
14. Young D, Fitzgerald K, Laursen L, Whitaker AK. Comparison of vaginal and buccal misoprostol after mifepristone for medication abortion through 70 days of gestation: A retrospective chart review. Contraception. 2022;115:62-6.
15. Varlas VN, Bostan G, Nasui BA, Bacalbasa N, Pop AL. Is misoprostol vaginal insert safe for the induction of labor in high-risk pregnancy obese women?. InHealthcare 2021 Apr 14 (Vol. 9, No. 4, p. 464). MDPI.
16. Mundle S, Lightly K, Durocher J, Bracken H, Tadas M, Parvekar S, Shivkumar PV, Faragher B, Easterling T, Leigh S, Turner M. Oral misoprostol alone, compared with oral misoprostol followed by oxytocin, in women induced for hypertension of pregnancy: A multicentre randomised trial. BJOG: An International Journal of Obstetrics & Gynaecology. 2024 Oct;131(11):1532-44.
17. Bracken H, Lightly K, Mundle S, Kerr R, Faragher B, Easterling T, Leigh S, Turner M, Alfirevic Z, Winikoff B, Weeks A. Oral Misoprostol alone versus oral misoprostol followed by oxytocin for labour induction in women with hypertension in pregnancy (MOLI): protocol for a randomised controlled trial. BMC pregnancy and childbirth. 2021 Dec;21:1-8.
18. Zhang L. Efficacy of Misoprostol in the Treatment of Postpartum Haemorrhage in Hypertensive Syndrome During Pregnancy. Academic Journal of Medicine & Health Sciences. 2023 Aug 20;4(8):43-8.
19. Ibrahim MA, Abdel Dayem HM, Abdelrhman AA, Abo El-Khir DH. Effect of Isosorbide Mononitrate and Misoprostol for Cervical Ripening in Induction of Labor. The Egyptian Journal of Hospital Medicine. 2021 Apr 1;83(1):862-8.
20. Rahimi M, Haghighi L, Baradaran HR, Azami M, Larijani SS, Kazemzadeh P, Moradi Y. Comparison of the effect of oral and vaginal misoprostol on labor induction: updating a systematic review and meta-analysis of interventional studies. European journal of medical research. 2023 Jan 27;28(1):51.
21. Shah SR, Vhora H. Comparison of Induction of Labour with Mifepristone and Misoprostol at Term V/S. Induction with Misoprostol Alone. WJ Heal Med. 2024;2(2):1020.