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## Determination of vaginal pH and its role on the efficacy of Dinoprostone gel for labour induction/cervical ripening

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### Abstract

**Background:** The change in vaginal pH has an effect on preterm delivery and it suggests that there may be association of vaginal pH with cervical ripening/change in Bishop score. The aim of this study is determination of vaginal pH and its role on the Dinoprostone gel effect for cervical ripening.

**Subjects and Methods:** This is hospital based prospective observational study done on 50 pregnant women admitted in labour room for labour induction and fulfilling inclusion/exclusion criteria at Obstetrics and Gynaecology department, RMMCH. After initial Bishop score assessment and vaginal pH, all women received Dinoprostone gel intracervically (0.5mg) for cervical ripening. Group 1 included patients with vaginal pH <4.5 and group 2 included with vaginal PH  $\geq$ 4.5. Their clinical outcomes were noted. The significance of association was calculated by Chi-square test. Results: The mean vaginal pH was  $4.43 \pm 0.62$  (range 3-6). Multiparous women were associated with higher pH. Bishop score after PGE<sub>2</sub> gel induction, mode of delivery and induction to delivery interval were significant in vaginal pH  $\geq$ 4.5 (group 2). No significant difference were noted between two groups in relation with age, gestational age and Bishop score before PGE<sub>2</sub> gel induction, time taken to enter into active phase.

**Conclusion:** vaginal pH is influenced by parity and vaginal pH by itself has an effect on cervical ripening. Thus patients with higher vaginal pH had good response to PGE<sub>2</sub> gel resulting in successful induction by cervical ripening/vaginal deliveries.

**Keywords:** Dinoprostone gel, vaginal pH, Modified Bishop score

### Introduction

Induction of labour is defined as an intervention designed to artificially initiate and perpetuate uterine contractions with progressive dilatation and effacement of the cervix and leading to delivery of the baby. There are various methods for labour induction, one of the methods of induction is with prostaglandins and oxytocin or by artificial rupture of amniotic membranes. Successful induction should result in delivery of the baby without maternal and neonatal complications.

Cervix is made of few smooth muscle cells and obtains its rigidity from collagen bundles and proteoglycans. Cervical ripening is the disorganization of collagen bundles mainly by collagenase. Cervical pH in pregnancy usually varies between 6 and 7 whereas vaginal pH is maintained between 3.8 and 4.8. Vaginal pH is an acidic environment mainly from glycogen metabolism by lactobacillus producing lactic acid.

Administration of exogenous prostaglandins causes enzymatic modification that promote collagen breakdown followed by rearrangement of collagen fibres and alter the extracellular matrix, which results in cervical ripening [1]. Prostaglandins are important for cervical ripening due to its collagenolytic properties in addition to it, it also sensitizes the myometrium to oxytocin. The diminished solubility of prostaglandins in aqueous solution at low pH is due to its acidic nature [2]. The efficacy of the drug is influenced by the acidity of the vagina and this results in varying clinical outcomes.

M. Norman *et al.* studied the cervical connective tissue metabolism from cervical biopsies between non-pregnant and pregnant cases. The proteoglycan concentration found in pregnant cervix is approximately one half that of non-pregnant cervix indicating proteoglycan turnover was significantly increased in pregnant cervical tissue. After prostaglandin induction it was found that there was a decline in cervical resistance which was brought about by decrease in sulfated glycosaminoglycans that in turn weakens the interfibrillar interactions because of

decrease in electrostatic interactions. The involvement of matrix metalloproteinases (MMP) i.e. MMP-2 and MMP-9 in the cervical ripening process has been indicated in cervical ripening [3, 4].

In-vitro studies have been conducted on the effect of vaginal pH on release of PGE<sub>2</sub> from vaginal and endocervical preparations where lactose based vaginal tablet had enhanced released at low pH while for triacetin gel preparation, PGE<sub>2</sub> release was decreased at lower pH, while the starch based gel preparations has an optimal release at pH 5.4 [5].

Studies shows that absorption of drug and degree of ionization of the drug is affected by vaginal pH which results in variable clinical responses [6, 9]. Even in preterm delivery, change in vaginal pH plays a role which suggests its effect on cervical ripening [7, 8].

The aim of the study is to determine the vaginal pH and its influence on the effect of dinoprostone gel which would improve the patient selection for PGE<sub>2</sub> and reduce the incidence of failed induction with PGE<sub>2</sub> gel.

**Materials and Methodology**

This is a prospective observational study of pregnant women who had indication for cervical ripening/induction of labour in the Department of Obstetrics & Gynaecology, Rajah Muthiah Medical College and Hospital, Chidambaram for One year-October 2019 to October 2021 after getting approval by the Institutional Ethic Committee of Rajah Muthiah Medical College & Hospital. Inclusion criteria were (1) An unfavourable cervical Bishop score of ≤ 5, (2) Singleton pregnancy with vertex presentation and no contraindication to vaginal delivery. (3) Assuring fetal heart rate

**Exclusion criteria included**

(1) prostaglandin hypersensitivity (2) Placenta praevia (3) Suspected chorioamnionitis (4) Parity of >3 (5) A previous cesarean delivery or a scarred uterus (6) Induction of labor previously tried in this pregnancy (7) Cephalopelvic disproportion. 8) Previous caesarean delivery or a history of uterine surgery.

Subjects who fulfilled the above mentioned criterias were observed in this study after giving informed and written consent. The cases which satisfy the inclusion criteria was examined per speculum, and vaginal pH value will be assessed by using pH indicator paper (both broad & narrow spectrum by ph paper, Sigma Chemical company, st. Louis, USA). by placing on the lateral vaginal wall until it becomes wet. Colour change in the pH strips were compared with the colorometric scale of the manufactures and those findings was noted

Following pH assessment, vaginal examination was done to assess the Bishop’s score by examining the cervical dilatation, cervical effacement/length, cervical consistency, cervical position and station of the presenting part. Each component was given a score of 0-2 or 0-3. The highest score is 13 and <5 indicates unfavourable cervix, which needs induction. PGE<sub>2</sub> gel 0.5 mg placed intracervically. Following application, the patient was informed to be in a recumbent position for minimum of 30 minutes and continuous monitoring of the patients was done. Patient was reassessed after 6-8 hours. Based on uterine contractions and Bishop score, either PGE<sub>2</sub> gel was repeated (2 doses at maximum) or augmentation of labour was done as per labour theatre protocol [10].

The subjects were divided into two groups one with vaginal pH (<4.5) and the other with vaginal pH (≥4.5) and comparison and

analysis of Age, gestational age, parity, Pre-induction Bishop score, need for augmentation, time taken to enter into active phase of labour and the mode of delivery between two groups. The induction to delivery interval, indication for caesarean and LSCS rates, maternal complications, fetal outcomes in terms of birth weight and APGAR score were noted and tabulated. A statistical package SPSS version 17.0 was used to do the analysis and P value <0.05 was considered and significant.

**Results**

A total of 50 women who need cervical ripening with Bishop score ≤5 were taken for this study.

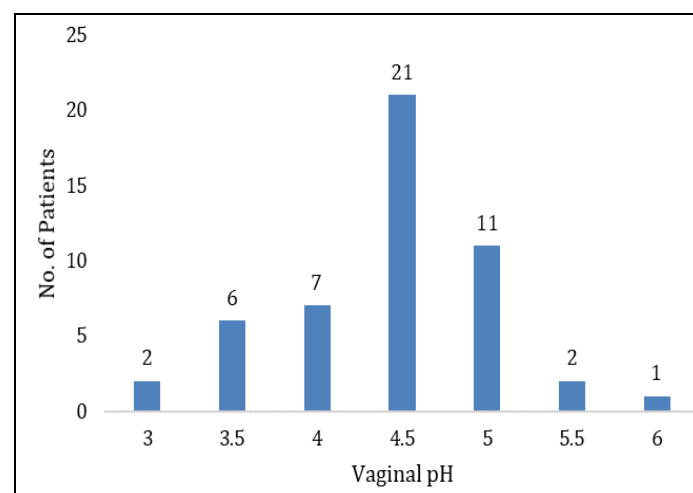
Group 1 had patients with vaginal <4.5 and group 2 had patients with ≥4.5.

Baseline characteristics were shown in table 1. There was no statistically significant association between the two groups with respect to maternal age, gestational age and bishop score prior induction.

**Table 1:** Baseline characteristics

Baseline characteristics	Group	N	Mean	Std. Deviation	t value	P value
Age	<4.5	15	25.33	3.88	0.67	0.504
	≥4.5	35	24.65	2.95		
Gestational age (weeks)	<4.5	15	38.70	0.96	0.91	0.364
	≥4.5	35	38.20	2.15		
parity	<4.5	15	1.33	0.48	2.17	0.035*
	≥4.5	35	1.65	0.48		
Bishop score prior induction	<4.5	15	2.86	1.06	1.83	0.073
Vaginal pH	<4.5	15	3.66	0.36	9.58	
	≥4.5	35	4.75	0.37		

There was significant association between vaginal pH and parity. Multiparous women had a vaginal pH ≥4.5.

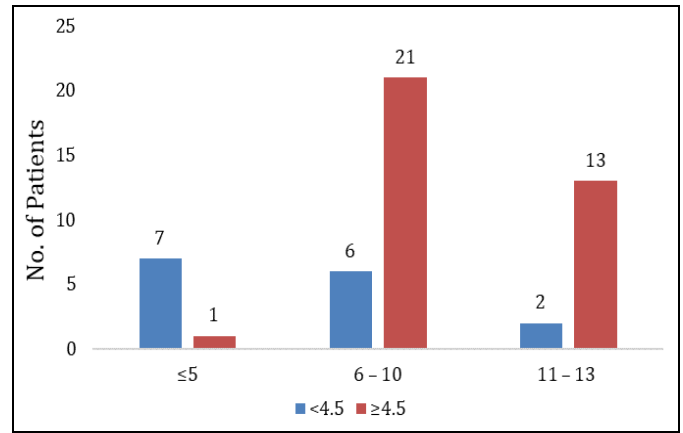


**Fig 1:** Frequency of vaginal pH

**Table 2:** Comparison of labour outcomes

Bishop score after PGE <sub>2</sub> first dose	<4.5	15	6.46	3.09	5.05	0.000**
	≥4.5	35	9.97	1.79		
Bishop score after PGE <sub>2</sub> gel second dose	<4.5	7	6.28	3.59	1.21	0.260
	≥4.5	3	9.33	3.78		
Time taken to enter into active phase of labour	<4.5	15	3.86	6.02	1.84	0.072
	≥4.5	35	6.22	3.07		
Induction Delivery Interval (hrs)	<4.5	15	14.20	10.83	2.54	0.014*
	≥4.5	35	9.08	3.41		

There was difference of significance noted between two groups in comparison of vaginal pH with Bishop score after first dose of PGE<sub>2</sub> gel and induction to delivery interval ( $p < 0.001$  and  $p < 0.05$  respectively). Patients with vaginal pH  $\geq 4.5$  had higher mean Bishop score after PGE<sub>2</sub> gel induction and also less induction to delivery

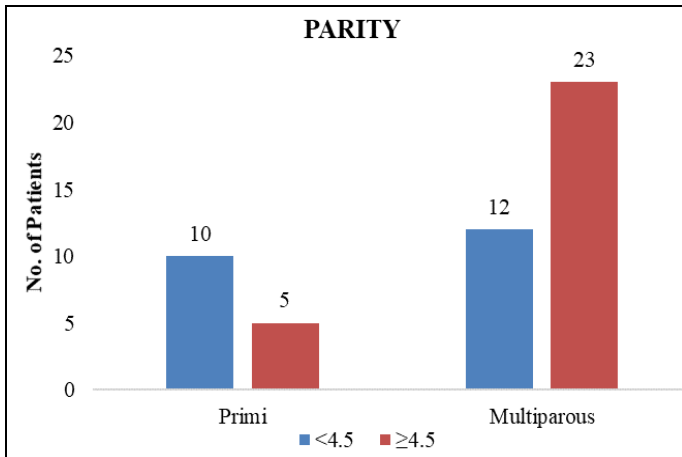


**Fig 3:** Comparison of vaginal pH with Bishops score after first PGE<sub>2</sub> gel

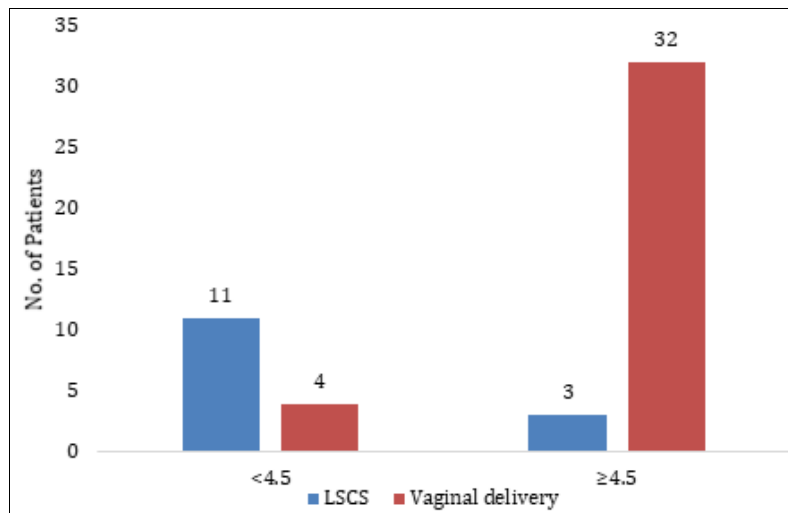
**Table 3:** Comparison of vaginal pH and Mode of delivery

Mode of delivery	<4.5	≥4.5
LSCS	11	3
Vaginal delivery	4	32
Total	15	35

Chi square test = 21.84,  $p = 0.000^{**}$ , statistically significant



**Fig 2:** Comparison of Vaginal pH with parity



**Fig 4:** Comparison of vaginal pH and Mode of delivery

**Discussion**

In our study, 50 patients were included in the age group of 18 to 35 years. They were categorised into two groups. Group 1  $< 4.5$  and group 2  $> 4.5$ . The mean age of the study group being 24.86 years and the mean gestational age was 38 weeks+ 4 days. The most common indication for induction was oligohydramnios followed by postdatism and gestational hypertension complicating pregnancy.

Majority of the patients (38%) in the study group were induced from 38 to 40 weeks. About 34% were induced at the gestational age of  $> 40$  weeks to 41 weeks + 1 day interval. The distribution of vaginal pH among patients studied showed that the vaginal pH was in the range of 3 to 6. The mean vaginal pH in the study group was found to be  $4.43 \pm 0.62$ . 20 patients had a pre-induction Modified Bishop Score of 3. The median Modified Bishop Score was 3.

After the first PGE<sub>2</sub> gel application, 18% had a modified Bishop score of  $\leq 5$ , 52% with a score of 6-10 and 30% had a score of 11-13. The need for second dose of PGE<sub>2</sub> gel and augmentation between two groups was not statistically significant.

The average time to entry into active phase of labour of both

groups was 5 hours 52 minutes. The induction to delivery interval in group 1 was 14 hours 20 minutes and group 2 was 9 hours 08 minutes which is statistically significant ( $p = 0.014$ ). On analysing the mode of delivery in our study group, 36 patients had vaginal delivery of which 4 delivered by outlet forceps and 14 patients underwent LSCS of which 8 patients underwent LSCS in view of fetal bradycardia.

Based on post operative complications, 94% had no complication reported. 4% had post-partum haemorrhage and 2% had abruption placenta.

The mean birth weight of the babies born was found to be 2.6 kg. About 20 patients were in the range of 2.5 to 3 kg. In this study 54% of the babies had a 1 minute APGAR of 7 and 44% of the babies had a 5 minute APGAR of 8. Neonatal intensive care unit (NICU) admission was needed for 12% of babies in view of perinatal Asphyxia (8%) and perinatal asphyxia complicated by HIE 2 (4%).

In the previous study by Goswami *et al*, there was no statistically significant association between the age, parity and gestational age but the difference in mean initial Bishop Score was slightly significant. A statistically significant change was

found in Bishop Score after PGE<sub>2</sub> gel over 12 hour, time taken to enter active phase, induction to delivery interval and mode of delivery.

In previous study by Kurian *et al*, there was significant association seen in higher vaginal pH (>5) in comparison with

parity, Bishop score prior Induction, dosage of gel but the change in the Bishop score over 6-8 hours of induction was not assessed. There was no significant association found in vaginal pH influencing the time taken to enter active phase of labour and incidence of caesarean section.

**Table 3:** Summary of comparison of the present study with previous conducted studies

Year of study	Study conducted by	PGE <sub>2</sub> form used in the study	Number of subjects in the study	Association of vaginal pH and age	Association of vaginal pH and parity	Association of vaginal pH and Bishop score prior induction	Association of vaginal pH and time taken to enter into active phase of labour
2002	Ramsey <i>et al</i> .	gel	32	A	A	A	B
2011	Singh U <i>et al</i> .	gel	45	A	A	A	A
2015	Goswami <i>et al</i> .	gel	110	B	B	A	A
2016	Kurian <i>et al</i> .	gel	200	B	A	A	B
Present study		gel	50	B	A	B	B

In our study, the distribution of vaginal pH (<4.5 and ≥4.5) between primi and multiparous showed that there was a statistically significant difference with  $p < 0.05$ . Patients with higher parity has a higher vaginal pH (≥4.5).

In previous studies, there was significant association between vaginal pH and Bishop score prior induction. In our study, Comparison of Vaginal pH with Bishop Score before PGE<sub>2</sub> induction showed that there was no statistically significant difference but who were reported with vaginal pH of ≥4.5 found to have statistically higher Bishop score after the gel administration and their time taken to enter into active phase reduced to less than 10 hours in group 2. In the previous study by Singh u *et al*. also although there has been a difference in duration of assessment of Bishop score, had similar significant association between the vaginal pH and change in the Bishop score over 18 hours.

There was statistical significance noted between two groups, observation noted was group 2 had taken 6 to 10 hours induction to delivery interval compared to group 1 where majority had taken more than 10 hours. A total of 50% patients with a vaginal pH of 4.5 to 5 delivered vaginally. On the other hand 20% of patients with a vaginal pH of 3.5 to 4 underwent LSCS. Hence higher the vaginal pH, the chance of normal delivery is increased when induced with PGE<sub>2</sub> gel.

Lyrenas *et al*. further noted that high vaginal pH (6.5-7.5) and therefore increased PGE<sub>2</sub> release did not equate to increased plasma concentrations of PGE<sub>2</sub> and its metabolites. Therefore, why vaginal pH affected the cervical priming but did not affect the labour outcomes in present study may be due to these findings that ionisation of PGE<sub>2</sub> in high pH might cause local effects, like change in Bishop score, and the diminishing of its absorption may decrease its systemic effects and therefore, absence of change in labor outcomes<sup>[11]</sup>.

The effect of vaginal pH on the efficacy of sustained-release PGE<sub>2</sub> vaginal insert could be better established if the vaginal insert had been moistened with solutions having different pH as in the previous studies<sup>[12]</sup>.

### Conclusion

Hence present study implies that cervical ripening is significantly affected by changes in vaginal pH and it also influences mode of delivery. The pH is important in terms of the design and the efficacy of vaginal drug delivery systems. Group 2 with higher vaginal pH, there is better change of bishop's score and shorter induction to delivery interval.

Parity influences vaginal pH. Group 2 with Vaginal pH ≥4.5 had less cesarean rates. Assessment of vaginal pH is a easily performed quantitative method in assessing the pre-induction favourability of the cervix. Hence this method would enable obstetricians to predict the success of outcome following

induction of labour and to select a safe and more efficient method of induction. Assessment of vaginal pH appears to be a better tool. Further research is required to find various agents that would increase the vaginal pH thereby creating a favourable environment for PGE<sub>2</sub> gel induction.

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