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A Prospective Study to Evaluate the Changes in Vaginal Cytology and its Correlation with Bishop's Scoring to Predict the Onset of Labor

Choudhary V[1], Sah S[2], Arya SB[3], Agarwal T[4], Agarwal N[5], Baghel J[6]

[2]Professor, Department of Obstetrics and Gynecology, Shri Ram Murti Smarak institute of Medical Sciences, Bareilly, Uttar Pradesh (Corresponding Author)

Abstract: ***Aim*** *To evaluate the vaginal cytological changes and its correlation with Bishop's scoring in predicting the onset of labor.* ***Material and Methods****: In our study 100 antenatal patients admitted in the labor ward of Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly in prelabor stage were enrolled and were subjected to vaginal cytology and Bishop's scoring.50 preterm patients (less than 37 weeks) were considered as control for comparison of vaginal cytology. The prelabor subjects were followed in early labor to correlate the cytological changes at onset of labor and duration of onset and progression into labor and also to determine validity of cytological changes against Bishops scoring in predicting labor onset.* ***Results****: In preterm group, it was observed that maximum number of cells/hpf were intermediate cells with cell number > 30/hpf at < 36 weeks gestation. Beyond 37 weeks there is alteration in ratio of progesterone to estrogen which reflects an increase in number of superficial cells decrease in intermediate cells and cluster cells. At onset of labor cervical changes leads to increase in Bishop's score, hence Bishop's score increases from prelabor to early labor group. The comparison between superficial cells on Pap smear and Bishop's score was statistically significant and had 83.83 % predictive value compared to bishop score in predicting labor onset within 3 days if superficial cells were > 30/hpf.* ***Conclusion****: Vaginal cytology and Bishop's score both can predict labor independently but Pap smear being an objective test has higher sensitivity and specificity compared to Bishop's score which is more a subjective test.*

1. Introduction

The onset of effective uterine contractions that lead to gradual effacement and dilatation of the cervix, resulting in the evacuation of the fetus, placenta, and membranes is known to as labor. The timing of onset of labor is variable and 80 % of cases deliver between 38 weeks and 41 weeks of which 60% cases delivers within a week in either direction from expected date of delivery.1 Maintenance of pregnancy and onset of labor is largely dependent on estrogen and progesterone, sex steroid hormone. Vaginal cytology is also directly influenced by hormonal changes. Cytologically three different cells numbers are seen based on serum concentration of estrogen and progesterone. Under effect of estrogen superficial cells increases and under effect of progesterone intermediate cells increases.2 Progesterone also causes clusters of mature folded intermediate cells called navicular cells and the number of clusters fluctuates with progesterone level.3 As a result, endocrine interpretation of a vaginal swab can forecast the start of labor and show a change in the cytologic smear. Cytology in pregnancy has not been given significant emphasis, although it is economical and of great importance and can be easily used and support the masses in low-resource environments.

Aim

To evaluate the vaginal cytological changes and its correlation with Bishop's scoring in predicting the onset of labor.

2. Material and Method

This was a prospective case study conducted in department of obstetrics and gynecology, SRMS IMS, Bareilly on 100 antenatal patients admitted in the labor ward in prelabor stage from Nov 2019 to April 2021.50 antenatal patients less than 37 weeks visiting OPD were considered as control for evaluating vaginal cytological changes.

Inclusion Criteria

1) Term singleton gestation (37-42 weeks POG)
2) Cephalic
3) latent labor

Exclusion Criteria

1) Multiple pregnancy
2) Antepartum haemorrhage
3) Premature rupture of membranes
4) Vaginal discharge
5) Tococlytic
6) Patient kept for elective cesarean section
7) Patient in advance labor

All patients were subjected to vaginal cytology and Bishop's scoring was done. The prelabor subjects were followed in early labor by vaginal cytology to correlate the changes. Bishop's score was done to compare the duration of onset and progression into labor and to determine validity of cytological changes. The smear was taken from upper one third of vaginal wall prior to digital examination with a sterile wooden spatula and smeared on a glass slide and then was fixed on alcohol for 20 minutes and stained according to Papanicolaou method. Three stains used in pap stain were –

- Hematoxylin stain
- OG – 6 stain
- EA-50

Steps of Pap smear-

1) Slide are immersed in 95% Ethanol for 15 minutes (Fixation)
2) Rinsed in tap water
3) Immersed in Gill Hematoxylin for 1-3 minutes

4) Rinsed in tap water
5) Dipped 10 times in 95% Ethanol
6) Kept in OG-6 stain for 1.5 minutes
7) Dipped 10 times in 95% Ethanol Immersed in EA-50 for 2.5 min
8) Dipped 10 times in 95% Ethanol
9) Immersed in 100 % Ethanol for 1 minute
10) Cleared with xylene
11) Mounted with permanent mounting medium
12) Examined under high power field for-

Number of intermediate cells per cluster
Number of superficial cells
Number of cluster cells

Cervical scoring was based on modified Bishop's scoring criteria. The patient's vaginal smear for cytology and repeat Bishop's score was taken in prelabor and at onset of labor which was defined as occurrence of regular, painful uterine contractions resulting in progressive cervical effacement and dilatation. Date and time of onset of labor was noted.

3. Results

Table 1: Demographic characteristics of subjects

Demographic		Preterm (N=50)	Prelabor (N=100)
Age	Mean± SD	29.18± 3.03	25.9±3.50
Parity	G1	21 (42%)	55 (55%)
	G2	19 (38%)	37 (37%)
	≥ G3	10 (20%)	8 (8%)
Gestational age	35-35+6 weeks	22 (44%)	5 (5%)
	36-36+6 weeks	28 (56%)	2 (2%)
	37-37+6 weeks	0	26 (26%)
	38-38+6 weeks	0	33 (33%)
	39-39+6 weeks	0	20 (20%)
	≥40 weeks	0	14 (14%)

Both the groups were comparable with respect to demographic variables.

Table 2: Comparison of superficial cells and intermediate cells in preterm, prelabor and early labor

No. of cells	PRETERM		PRELABOR		EARLY LABOR	
	Superficial cells	Intermediate cells	Superficial cells	Intermediate cells	Superficial cells	Intermediate cells
<10	16 (32%)	0	0	7 (7%)	0	55 (55%)
10-19	30 (60%)	1 (2%)	9 (9%)	62 (62%)	0	42 (42%)
20-29	4 (8%)	3 (6%)	23 (23%)	23 (23%)	9 (9%)	3 (3%)
30-39	0	23 (44%)	55 (55%)	8 (8%)	30 (30%)	0
40-49	0	13 (26%)	10 (10%)	0	17 (17%)	0
>50	0	10 (20%)	3 (3%)	0	44 (44%)	0
TOTAL	50 (100%)	50 (100%)	100 (100%)	100 (100%)	100 (100%)	100 (100%)
MEAN±SD	13.8±4.6	41.2 ±9.6	28.5±9.2	17.2±4.2	42.9±7.1	12.8±2.9
P value	<0.0001		<0.0001		<0.0001	

The number of superficial cells increased as the pregnancy advanced from preterm to prelabor to early labor with mean number of superficial cells 13.8±4.6, 28.5±9.2, 42.9±7.1 /hpf respectively for three groups. As gestational age approaches towards labor a decrease in intermediate cells occur with more than half of subjects ie (55 out of 100) having less than 10/hpf in early labor. Thus a mean decrease of 41.2±9.6 to 12.8 ±2.9 occurred from preterm to early labor.

Table 3: Comparison of clusters in preterm prelabor and early labor

Number of clusters	Preterm	Prelabor	Early Labor	
<5	0	56 (56%)	85 (85%)	**P VALUE <0.001**
5-9	1 (2%)	35 (35%)	15 (15%)	
10-14	35 (70%)	9 (9%)	0	
15-20	14 (28%)	0	0	
TOTAL	50 (100%)	100 (100%)	100 (100%)	
Mean±SD	13.2±2.4	6.3±1.9	3.7±1.3	

On comparing the three groups the number of clusters cells decreased from preterm to pre labor with mean value 13±2.4 to 6.3±1.9 which further decreased to 3.7± 1.3 in early labor.

Table 4: Comparison of intermediate cells and superficial cells according to gestational age

Gestation age	No of subjects	Number of cells/hpf											
	N=150 (preterm+ prelabor)	<10		10-19		20-29		30-39		40-49		>50	
		Intermediate	superficial	Intermediate	superficial	Intermediate	superficial	Intermediate	superficial	Intermediate	superficial	Intermediate	superficial
35-35+6 wk	27	0	7 (25.92%)	1 (3.70%)	16 (59.25%)	1 (3.70%)	4 (14.8%)	18 (66.66%)	0	7 (25.92%)	0	0	0
36-36+6 wk	30	0	9 (30%)	7 (23.33%)	16 (53.33%)	2 (6.66%)	5 (16.66%)	5 (16.66%)	0	6 (20%)	0	10 (33.33%)	0
37-37+6 wk	26	4 (15.38%)	0	9 (34.61%)	2 (7.69%)	9 (34.61%)	1 (3.84%)	4 (15.38%)	16 (61.53%)	0	5 (19.23%)	0	2 (7.69%)
38-38+6 wk	33	2 (6.06%)	0	19 (57.57%)	2 (6.06%)	8(24.24%)	6 (18.18%)	4 (12.12%)	19 (57.57%)	0	5 (21.73%)	0	1 (4.34%)
39-39+6 wk	20	0	0	16 (80%)	1 (5%)	4(20%)	7 (35%)	0	12 (60%)	0	0	0	0
>40 wk	14	1 (7.14%)	0	11 (78.57%)	2 (14.28%)	2 (14.28%)	4 (28.57%)	0	8 (57.14%)	0	0	0	0
Total	150	7 (4.66%)	16 (10.66%)	63 (42%)	39 (26%)	26 (17.33%)	27 (18%)	31 (20.66%)	55 (36.66%)	13 (8.66%)	10 (6.66%)	10 (6.66%)	3 (2%)

As period of gestation increases the number of superficial cells increases from < 30/hpf being predominant at gestational age < 37 weeks to maximum at term prior to onset of labor, on contrary beyond 37 weeks intermediate cells decreases with 85.7 % cases having intermediate cells <20/hpf at gestational age >40 weeks thus showing an alteration in estrogen and progesterone ratio.

Table 5: Comparison of Bishop's score in prelabor and early labor with onset of labor in days

Bishop's score		PRELABOR						Early labor				
	n	Onset of labor in days					n	Onset of labor in days				
		1	2	3	4	≥5		1	2	3	4	≥ 5
1-2	12	0	0	0	0	12	0	0	0	0	0	0
3-4	64	0	2	28	34	0	0	0	0	0	0	0
5-6	24	10	7	7	0	0	24	10	7	7	0	0
7-8	0	0	0	0	0	0	41	23	10	8	0	0
9-10	0	0	0	0	0	0	35	35	0	0	0	0
>10	0	0	0	0	0	0	0	0	0	0	0	0
total	100						100					

The mean duration of labor onset, among pre-labor subjects the patients with score 1-2 was after 5 days while those with score of 5-6 progressed in active labor within 3 days. The mean bishop score improved from 5.38±1.3 in pre-labor group to 9.63±2.1 in early labor.

Table 6: Comparison of duration of labor onset based on superficial cells and Bishop's Score

Types of cells	Onset of labor in days							
	Number of cells	Number of cases	1 day	2 days	3 days	4 days	≥ 5 days	
Superficial cells in Pap smears	<10	0						
	10-19	9 (9%)	2 (22.22%)	4 (44.44%)	1 (11.11%)	2 (22.22%)	0	
	20-29	23 (23%)	4 (17.39%)	9 (39.13%)	8 (34.70%)	2 (8.69%)	0	
	30-39	55 (55%)	28 (50.09%)	16 (26.09%)	9 (16.36%)	2 (3.63%)	0	
	40-49	10 (10%)	6 (60%)	2 (20%)	2 (20%)	0	0	
	>50	3 (3%)	2 (66.66%)	1 (33.33%)	0	0	0	
Total		100						
Bishop's score		Number of cases	1 day	2 days	3 days	4 days	≥ 5 days	
	1-2	12 (12%)	0	0	0	0	12 (100%)	
	3-4	64 (64%)	0	2 (3.12%)	28 (43.75%)	34 (53.12%)	0	
	5-6	24 (24%)	10 (41.66%)	7 (29.16%)	7 (29.16%)	0	0	P value <0.0001
	7-8	0	0	0	0	0	0	
	9-10	0	0	0	0	0	0	
	>10	0	0	0	0	0	0	
Total		100						

In prelabor group those with superficial cells with >30/hpf (ie 66. % subjects) approximately 97 % went into spontaneous active labor within 3 days.

Table 7: Diagnostic accuracy of superficial cells and Bishop's score with onset of labor among prelabor group within 3 days

Parameter	True positive	True negative	False positive	False negative	PPV	NPV	Sensitivity	Specificity
Bishop's	24	12	34	30	41.37	28.57	44.44%	26.08%
Superficial cells	57	9	11	23	83.82	28.12	71.25%	45.00%

Superficial cells on pap smear had 83.82% PPV in predicting onset of labor within 3 days compared to only 41.37% PPV of Bishops score.

4. Discussions

The present study was conducted to evaluate the changes occurring in vaginal cytology at different gestational age and also to determine the utility of these findings in predicting labor onset as compared to Bishop's score.

Pap smear detect the ratio of superficial and intermediate cells on vaginal cytology. Superficial cells is under influence of estrogen whose ratio increases during labor by activation of fetal HPO axis leading to the synthesis of myometrial receptors of oxytocin, it also causes prostaglandins release stimulating the synthesis of myometrial contractile protein to intensify which causes cervical ripening and induces uterine contraction.4 It was observed that at the onset of labor there was a significant increase in number of superficial cells. In preterm 32% subjects had superficial cells <10 /hpf while 60% had cells between 10-19 / hpf. None of the preterm subject had superficial cells > 30/hpf whereas with advancing pregnancy at prelabor stage an increase in superficial cells number was seen with no subject having superficial cell <10/hpf and maximum with cells >30/hpf, out of which 55% had superficial cells between 30 – 39/hpf and 3 % with >50/hpf. The number of superficial cells further increased in early labor with only 9 % subjects having < 30 cells/hpf and about 44 % with superficial cells > 50cells/hpf. We observed that as period of gestation increases the superficial cells number/hpf also increases with 59.25% subjects having cells between 10-19 at gestational age 35-35+6 week to 57.14 % subjects with cells between 30 – 39 at gestational age beyond 37 weeks. Findings of our study coincides with study of Dhingra J. et al (2016) which showed increase in superficial cells from prelabor to onset of labor with mean 45.09±8.23 and 54.37±5.15 respectively. The findings are also in accordance with the study conducted by Hammond M. D. (1965) where maturation index showed superficial cells were predominantly less than 30 cells/hpf at less than 37 weeks gestation and > 30 cells/hpf beyond 37 weeks gestation.5, [6]

Intermediate cells is under the influence of progesterone which is helpful in maintaining uterine quiescency and cervical competency thus help in continuation of pregnancy.4 We observe in our study that during the preterm period there is abundance of intermediate cells. At onset of labor, majority of intermediate cells lose their navicular form and are shed as flat, individual cells or tiny sheets. In our study number of intermediate cells in preterm subjects was > 30/hpf in 92% cases, of which 46% had cells between 30 – 39 /hpf and 20% had > 50 cells/hpf. None of the subject had intermediate cells <10/hpf. When the pregnancy advances to term the number of intermediate cells/ hpf decreased with majority of subjects in prelabor having intermediate cells between 10 – 19/hpf i. e.62% while in early labor 55% had intermediate cells <10/hpf. Only 8% subjects of prelabor had intermediate cells >30/hpf whereas none of the subject in early labor had intermediate cells > 30/hpf. As gestational age advanced intermediate cells number decreased from 92.5% subjects having intermediate cells >30/hpf at 35-35+6 weeks period of gestation to 85-88% subjects having intermediate cells <30/hpf between 37-38+6 and 80-85% subjects having intermediate cells <20/hpf at >39 weeks gestation. Our results coincided with the result of the study conducted by Dhingra J. et al (2016) where mean intermediate cells in prelabor were 11.78±2.82 and at onset of labor was 6.26 ±1.346 with a significant p value, A similar result was also observed in Gowri et al (2011) study wherein vaginal cytology was followed from week 32 till the first stage of labor and the total intermediate cell value was employed as an indication of impending labor, with values of 90.35 +/-0.0863, 89.41 +/-0.1934, 81.25 +/-0.0558, and 78.75 +/-0.0995 at week 38, 39, and 40, respectively.6, [7]

In our study in early labor group, the average clusters were 3.7±1.3 and 6.3±1.9 in early and prelabor group respectively as compared to 13.2±2.4 in the preterm group. Study conducted by Dhingra J et al (2016) had also observed similar results i. e. a decrease in mean clusters from pre-labor being 16.01±3.66 to 5.23±1.319 at onset of labor. As the pregnancy advances the intermediate cells loose their morphology due to withdrawal of progesterone hormone and become sheet like called navicular cells or the cluster cells.8 The curling property of cells is reduced and the size of these cluster cells as well as the number of cluster cells decrease at onset of labor.4 Cluster cells are under the influence of progesterone hormone and are found in abundance in smears of patients on medroxyprogesterone acetate, luteal phase of menstrual cycle and during menopause.4 The results of our study also co-incides with a study conducted by Aiket M et al (1959) where "preterm" smear showed predominance of navicular cells arranged in clusters while "At term smear" had tiny clumps and there was a gradual break of large clumps into small clumps with progress of pregnancy in 95% of cases. Lichtfus (1959) also recorded alterations in cell morphology in 97.3% cases at term and 2.7% cases prior to term who went in spontaneous labor within 5 days in a study conducted on 369 subjects. These changes were also demonstrated by study conducted by Pandit A A, Kalgutkar A K (1986) who discovered big clumps of intermediate cells prior to labor and single intermediate cells or small clumps of intermediate cells during the onset of labor.9, [10, 11]

Bishop's score is a clinical score to see the status of cervix given by Edward Bishop, MD (1960) to access the cervix and predict onset of labor. The scoring system utilizes cervical dilatation, position, length, consistency of the

cervix, and fetal station.1[2] In our study subject in the early labor group had a mean score of 9.63± 2.1 with 41% and 35% having cervical score of 7-8 and 9-10 respectively. Our study was in agreement with study done by Dhingra J et al (2016) with Bishop's score improving from prelabor to onset of labor from 3.66±0.47 to 4.54 ±0.99.6

The mean duration of labor onset in the prelabor group in our study for patients with Bishop score 1-2 was beyond a period of 5 days but with Bishop's between 3-4, 28 subjects out of 64 had onset within 3 days while rest has labor onset within 4 days. As the Bishop's score improved to 5-6, onset occurred within 3 days. The findings of our study coincides with the results of study conducted by Harrison et al (1977), who discovered a considerable increase in scores and a link between the Bishop's score and the length of labor wherein 87% subjects in their study with a score of 7 or above delivered in less than 9 hours, while only 44% patients with a score of 4 or lower delivered within this time.1[3] This variation in labor onset may probably be due to subjective variation in findings. While comparing the duration of onset of labor based on presence of superficial cells, it was observed that subjects with superficial cells beyond the range of >50 cells /hpf had onset of labor within 2 days while those with superficial cells >30/hpf had onset of labor within 3 days. The p-value for superficial cells and Bishop's score in prelabor group was found to be statistically significant.

Superficial cells number in pap smear in our study in prelabor group had a sensitivity of 71.25% compared to Bishop score with 44.44% sensitivity whereas the specificity for Bishop's score and superficial cells in pap smear was found to be 26.08% and 45.00 % respectively in predicting labor within 3 days. Similar sensitivity and specificity for pap smear was found in study conducted by Mojgan k et al (2015) with sensitivity and specificity of pap smear being 55.3% and of 77.7% for predicting onset of labor within 3 days, Naucler et al (2011) found the sensitivity and specificity of pap smear to be 55.4% and 96.8% in predicting labor onset within 3 days whereas Diny G E Kolman (2000) et al found Bishop's score sensitivity 61% and specificity 53% in predicting labor onset within 3 days. Ahmad et al (2000) found 78.87% and 82% sensitivity and specificity of Bishop's score in predicting labor onset within 3 days.1[4, 15]

5. Conclusion

Timing of onset of labor is variable and depends on various physiological changes occurring on uterus and reproductive tract brought by hormonal influence. The mean intermediate cells to superficial cells ratio decreases from preterm to prelabor and further in early labor. Thus vaginal cytology showing intermediate cells > 30/hpf indicate preterm pregnancy while if superficial cells are> 30/hpf indicate term pregnancy. As superficial cells increases at term, it also predict onset of labor. Patients with superficial cells 40 – 49 /hpf or above have onset of labor mostly within 1 day, while those with superficial cells <30/hpf usually have onset of labor after 2 days.

Hence vaginal cytology is simple and inexpensive way which helps to predict onset of labor more reliably as compared to Bishop's score which is more subjective having more chance of error. The sensitivity and specificity of cytology is found higher compared to Bishop's score.

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