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RESEARCH ARTICLE

To Study the Vaginal Cytological Changes in Term Pregnant Women and to Determine its Role in Predicting the Onset of Labor

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ABSTRACT

Introduction: To study the vaginal cytological changes in pregnant women and to determine its diagnostic accuracy in predicting the onset of labor.

Material and methods: This prospective case study was conducted in the Department of Obstetrics and Gynecology, SRMS IMS, Bareilly on 100 antenatal patients admitted at term (37–42 weeks). Vaginal cytology was studied in subjects in the pre-labor stage and these subjects were followed in early labor.

Results: As the gestation period increases, there is an alteration in vaginal cytology under hormonal change. Due to a decrease in progesterone hormone at term, the number of intermediate cells decreases and that of superficial cells increases under the effect of estrogen hormone. Cluster cells also decrease. The sensitivity and specificity of superficial cells was 76.25 and 45%, respectively in predicting labor onset within 3 days.

Conclusion: Progesterone maintains pregnancy and is evidenced by increased intermediate cells. The mean intermediate cells to superficial cells ratio decrease from term to pre-labor and further in early labor. Thus vaginal cytology showing intermediate cells > 30/hpf indicates preterm pregnancy, while if superficial cells are> 30/hpf indicates term pregnancy.

Keywords: Onset of labor, Term pregnancy, Vaginal cytology

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INTRODUCTION

Maintenance of pregnancy and labor onset largely depends on progesterone and estrogen hormone. Progesterone inhibits uterine contractions throughout the first several months of pregnancy. As the pregnancy enters its seventh month, progesterone levels plateau and then drop.[1] It is the change in estrogen: progesterone ratio rather than the decrease in the absolute concentration of progesterone, which is correlated with increased prostaglandin synthesis.[2] Cytologically, three different types of cells are seen based on serum concentration of estrogen and progesterone: superficial cells, intermediate cells, and basal cells. Under the effect of estrogen, superficial cells increase, and intermediate cells increase under the effect of progesterone. As progesterone maintains pregnancy, the ratio of intermediate cells increases compared to superficial cells, whereas during labor, progesterone level falls and hence superficial cells increase compared to intermediate cells. With the commencement of labor, the intermediate cells lose their morphology and are arranged in sheets of navicular cells called cluster cells. The significant hormonal effect at the onset of labor on the vaginal smear leads to decreased cluster cells.

The present study aimed to see the vaginal cytological changes in term pregnant women and determine its diagnostic accuracy in predicting onset of labor.

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MATERIAL AND METHODS

This prospective case study was conducted in the Department of Obstetrics and Gynecology, SRMS IMS, Bareilly on 100 antenatal patients admitted at term (37–42 weeks). Vaginal cytology was studied in subjects in the pre-labor stage and these subjects were followed in early labor.

Inclusion Criteria

- Term singleton gestation (37–42 weeks POG)
- Cephalic
- Latent labor

Exclusion Criteria

- Multiple pregnancies
- Antepartum hemorrhage
- Premature rupture of membranes
- Vaginal discharge

- Tocolytic
- The patient kept for an elective cesarean section
- Patient in advanced labor

All the subjects were subjected to vaginal cytology. The smear was taken from the upper one-third of the vaginal wall prior to digital examination with a sterile wooden spatula smeared on a glass slide, and then it was fixed in alcohol for 20 minutes and stained according to the Papanicolaou method. Three stains used in pap stain were

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

Steps of Pap Smear

- Slide are immersed in 95% Ethanol for 15 minutes (Fixation)
- Rinsed in tap water
- Immersed in Gill Hematoxylin for 1 to 3 minutes
- Rinsed in tap water
- Dipped 10 times in 95% ethanol
- Kept in OG-6 stain for 1.5 minutes
- Dipped 10 times in 95% ethanol immersed in EA-50 for 2.5 minutes
- Dipped 10 times in 95% ethanol
- Immersed in 100 % ethanol for 1-minute
- Cleared with xylene
- Mounted with permanent mounting medium
- Examined under high power field for
- Number of intermediate cells per cluster
- Number of superficial cells
- Number of cluster cells

The cut-off for superficial cells is 30/hpf for differentiation of preterm and term smear. For intermediate cells is 30/hpf and for clusters is <10/hpf (Figures 1-3).

RESULTS

Out of 100 patients, 7 were excluded as they had PROM after hospital admission.

At term, a significant increase in the number of superficial cells was observed, with 11 and 24% cases having <30 cells/hpf while 89 and 76% cases had >30 superficial cells/hpf at >37 weeks of gestation and >38 weeks period of gestation. However, the significance of superficial cells after 40 weeks period of gestation was found insignificant (Table 1).

The number of intermediate cells were found to be > 30/hpf in only 16% of cases beyond 37 weeks period of gestation and as the period of gestation increases, intermediate cells decrease to 13% at > 38 weeks period of gestation while beyond 39 weeks all cases had < 30 cells/hpf (Table 2).

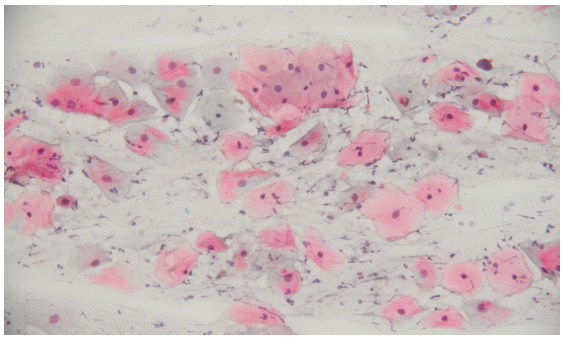

Figure 1: Superficial cells

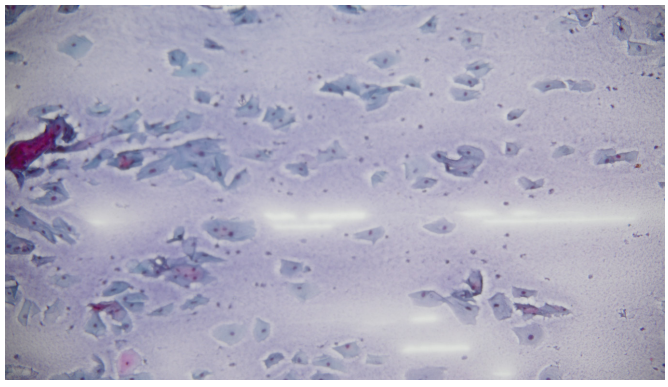

Figure 2: Intermediate cells

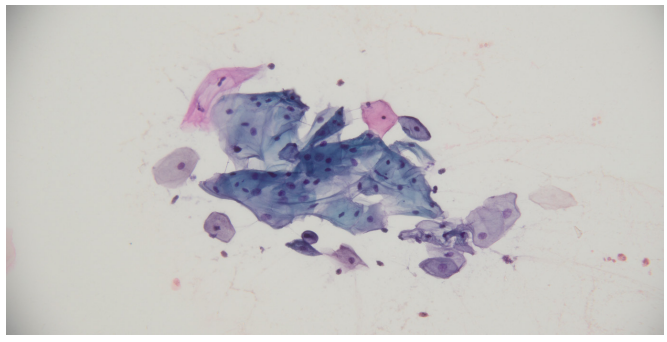

Figure 3: Cluster cells

Table 2: Comparison of intermediate cells according to gestational age (N=93)

Gestational age	*No of subjects*	*Number of cells/hpf*		*p-value*
	N=93	<30/hpf	>30/hpf	
37-37+6 week	26	22(84%)	4(16%)	0.003
38-38+6Week	33	29(87%)	4(13%)	0.0013
39-39+6Week	20	20(100%)	0	<0.001
>40 week	14	14(100%)	0	<0.001

Table 1: Comparison of superficial cells according to gestational age (N=93)

Gestational age	*No of subjects*	*Number of cells/hpf*		*p-value*
	N=93	<30/hpf	>30/hpf	
37-37+6 week	26	3(11%)	21 (89%)	0.0007
38-38+6week	33	8(24%)	24(76%)	0.002
39-39+6week	20	8(36%)	12(64%)	0.002
>40 week	14	6(42%)	8(58%)	0.4

Table 3: Comparison of clusters according to gestational age (N=93)

Types of cells			*Onset of labor in days*					
Superficial cells in Pap smears	*Number of cells*	*Number of cases*	*1 day*	*2 days*	*3 days*	*4 days*	*≥ 5 days*	
	<10	0						
	10-19	9(9%)	2(22%)	4(45%)	1(11%)	2(22%)	0	
	20-29	23(24%)	4(17%)	9(39%)	8(35%)	2(9%)	0	
	30-39	48(52%)	28(55%)	13(27%)	5(10%)	2(8%)	0	*p-value* <0.0001
	40-49	10(11%)	6(60%)	2(20%)	2(20%)	0	0	
	>50	3(4%)	2(67%)	1(33%)	0	0	0	
Total		93						

As the gestation period increases, there is a significant decrease in the number of cluster cells from >10 to <10/hpf with 84 % cases having less than 10/hpf cells at 37 and 38 weeks period of gestation (Table 3).

As the number of superficial cells exceeds 50 cells/hpf onset of labor occurred within 2 days in all cases while with <20 superficial cells /hpf 67% of cases had onset within 2 days and 33% of cases had onset of labor within 3 to 4 days and this was statistically significant (Table 4).

The true positive and true negative values for superficial cells in predicting onset of labor within three days were 57 and 9, respectively, with a sensitivity of 71.25% and specificity of 45% and a positive predictive value of 83.82 (Table 5).

DISCUSSION

Female hormones Estrogen and Progesterone affect various organs of the body with a major influence on the reproductive tract. However, the level do not remain constant and varies with the menstrual cycle and phases life. Thus, the ratio of cells seen on cytology during pregnancy can help predict delivery timing.[3] The present study was conducted to evaluate the changes occurring in vaginal cytology at different gestation age and determine the utility of these findings in predicting labor onset.[4]

Table 4: Comparison of duration of labor onset based on superficial cells

Gestational age (weeks)	*No of subjects*	*Number of cells/hpf*		*p-value*
	N=93	<10/hpf	>10/hpf	
37-37+6	26	22(84%)	4(16%)	0.003
38-38+6	33	28(84%)	5(16%)	0.003
39-39+6	20	12(60%)	8(40%)	0.3
>40	14	14(100%)	0	<0.001

The vaginal cytological index is based on the number of superficial, intermediate and basal cells. The increased number of superficial cells indicates estrogen activity, while increased intermediate cells indicate progesterone hormone activity. As the pregnancy advances from preterm to term gestation, a progesterone level change is reflected by vaginal cytology changes.[5] Progesterone hormone decreases at term, which further decreases at pre-labor and with the onset of labor, causing alteration in progesterone to estrogen ratio, thus leading to a decrease in intermediate cells and a comparative increase in superficial cells at term and thereafter.[6,7]

We observed that as the gestation period increases, the superficial cell number/hpf also increases with 89% of subjects with cells >30/hpf at gestational age beyond 37 weeks. The findings also follow the study conducted by Hammond M.D. (1965) where the maturation index showed superficial cells were predominantly > 30 cells/hpf beyond 37 weeks gestation.[8]

Intermediate cells is another cell type seen on the cytological smear of the vagina. These cells are under the influence of progesterone and are polygonal-shaped squamous cells. As gestational age advances, the number of intermediate cells decreases, with 84 to 87% of subjects having intermediate cells <30/hpf between 37-38+6 weeks of gestation. A similar result was also observed in Gowri *et al.* (2011) study, where in 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.[9]

With the commencement of labor, the intermediate cells lose their morphology and are arranged in clusters.

Table 5: Diagnostic accuracy of superficial cells in predicting onset of labor

Parameter	*True positive*	*True negative*	*False positive*	*False-negative*	*PPV*	*NPV*	*Sensitivity (%)*	*Specificity (%)*
Superficial cells	57	9	11	23	83.82	28.12	71.25	45.00

The characteristic changes of insufficient progesterone production on the vaginal smear are the disappearance of navicular clusters, the breaking of intermediate cell clusters and the replacement of intermediate cells by superficial squamous cells. Clusters cells decrease as the gestation advances, with 84% of the case having <10 cluster cells/hpf at gestational age beyond 37 and 38 weeks.

In our study all the subjects had onset of labor within 2 days as the number of superficial cells increased beyond the range of >50 cells /hpf while with <20 superficial cells /hpf, 67% cases had onset within 2 days and 33% cases had onset of labor within 4 days

In our study, the sensitivity of superficial cells was 76.25% and specificity was 45% in predicting labor onset within 3 days. Similar sensitivity and specificity for pap smear was found in a study conducted by Mojgan k *et al*.[10] (2015). The sensitivity and specificity of pap smear were 55.3 and of 77.7% for predicting onset of labor within 3 days Naucler *et al*.[11] found the sensitivity and specificity of pap smear to be 55.4 and 96.8% in predicting labor onset within 3 days.

LIMITATION

Contrary to the above studies, our study's specificity was less than sensitivity due to the small sample size. The diagnostic accuracy of superficial cells to predict the onset of labor is significant up to the expected date of delivery only.

CONCLUSION

The timing of the onset of labor is variable and depends on various physiological changes occurring on the uterus and reproductive tract brought by hormonal influence. Pregnancy is maintained by progesterone and is evidenced by increased intermediate cells. The mean intermediate cells to superficial cells ratio decrease from term to pre-labor and further in early labor.

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