

SALIVARY PROGESTERONE AS A BIOCHEMICAL MARKER TO PREDICT PRETERM BIRTH IN ASYMPTOMATIC HIGH RISK WOMEN

Gynaecology

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ABSTRACT

Background: Progesterone withdrawal in the initiation of labor is well established in sheep. Salivary progesterone is the biologically active form of progesterone and hence a correlation is hypothesized. **Objectives:** 1) To find out the role of salivary progesterone in prediction of preterm birth in asymptomatic high risk women 2) To compare it with transvaginal cervical length. **Materials and methods:** A total of 90 antenatal women satisfying the inclusion criteria were enrolled. Various demographic parameters, salivary progesterone and transvaginal cervical length were studied. **Results:** Salivary progesterone estimation at 24-28 weeks and then at 29-32 weeks in asymptomatic high risk antenatal mothers is a valuable predictor of preterm labor. Its sensitivity and specificity is comparable with the transvaginal cervical length. **Conclusion:** Salivary progesterone is a better predictor of preterm labor when compared to transvaginal cervical length, as it has better sensitivity and specificity. It is a non-invasive method and sample collection is easier.

KEYWORDS:

Salivary progesterone, transvaginal cervical length, preterm birth, biochemical marker.

INTRODUCTION

Prematurity is the most common cause of neonatal and infant mortality and morbidity. So, strategies for prediction and prevention of preterm labor is necessary. The tested biological markers included cervico-vaginal fetal fibronectin level, human chorionic gonadotropin (HCG) level and serum corticotropin releasing hormone (CRH) which lack acceptable validity, feasibility and availability. So a quicker, cheaper, simpler test with greater accuracy for predicting preterm labor is needed, so that one can avoid unnecessary tocolysis and take appropriate intervention or refer earlier to a tertiary care centre.

Goldenberg and colleagues (2008b) related pathogenesis of preterm labor to withdrawal of progesterone, initiation of oxytocin and activation of decidua. After 8 weeks, the syncytiotrophoblasts of the placenta secrete progesterone in progressively increasing levels which causes resistance to pressor agents in pregnancy. Progesterone increases uterine quiescence by decreasing the expression of contraction-associated proteins (CAPS) and inhibits the expression of connexin43. The progression of uterine quiescence and cervical competence into uterine activation and cervical ripening of parturition, is directly preceded by a fall in progesterone level.

This study was conducted with the aim to evaluate the role of salivary progesterone as a biochemical marker, to predict preterm birth in asymptomatic high risk women and to compare it with transvaginal cervical length. Various demographic variables were also assessed in this study.

MATERIALS AND METHODS

This prospective study was done in Institute of Obstetrics and Gynaecology, Egmore, Chennai from January 2015 to March 2016. Ethical clearance was obtained in December 2014. Informed written consent was obtained from all participants in the study. Asymptomatic women with singleton pregnancy with history of previous preterm birth or previous preterm prelabor rupture of membranes or late spontaneous miscarriage (20 to 28 weeks) were included in the study. Women with multiple gestation, uterine anomalies, medical disorders, bleeding gums, fetal growth restriction, on medications like progesterone and tocolytics and on cervical encirclage were excluded. The 90 enrolled antenatal women were subjected for a detailed history on demographic profile, medical disorders, obstetric history and antenatal complications in the present pregnancy. General examination and obstetric examination were also performed. Then, they were subjected to salivary progesterone estimation from 3 unstimulated samples by ELISA (DeMeditec kit) at 24 to 28 weeks and again at 29 to 32 weeks. At the same time, they were subjected to

transvaginal cervical length measurement. The data were evaluated using Receiver Operator Characteristic curve, chi-square test, t-test and linear regression curve.

RESULTS:

There was no correlation between age, pre-pregnancy height, weight and body mass index and preterm labor and neonatal complications. The risk of preterm labor was not increased in working women. Socio economic status did not have a significant impact on labor outcome and neonatal complications. Women with history of passive smoking (i.e., smoking among family members) were at a greater risk for preterm labor. Risk of NICU admissions were more in preterm deliveries, most common cause being respiratory distress syndrome followed by jaundice. Salivary progesterone estimation at 24-28 weeks and then at 29-32 weeks in asymptomatic high risk antenatal mothers was a valuable predictor of preterm labor when the cut off was fixed at ≤ 3903 pg/ml at 24-28 weeks and ≤ 2975 pg/ml at 29-32 weeks. Transvaginal cervical length measured at 24-28 weeks and then at 29-32 weeks, at the time of salivary progesterone estimation also, had similar sensitivity and specificity in predicting preterm labor when the cut off was fixed at ≤ 3.1 cm at 24-28 weeks and ≤ 2.9 cm at 29-32 weeks.

DISCUSSION:

A total of 90 antenatal women were enrolled in our study. Two women were diagnosed to have hyperglycemia in pregnancy between 29-32 weeks and were excluded from the study. Three women developed hypertensive disorder of pregnancy and were excluded from the study. One woman was diagnosed by ultrasound to have fetal growth restriction with oligohydramnios and was excluded from the study. Three women did not turn up between 29-32 weeks of gestation due to various reasons and were excluded from the study.

Receiver Operator Characteristic curve was drawn for salivary progesterone between 24-28 weeks and 29-32 weeks with respect to term and preterm deliveries. Salivary progesterone estimation done between 24 – 28 weeks, had a sensitivity of 100% and specificity of 94.2%, in predicting preterm labor when the criterion was fixed at ≤ 3903 pg/ml. The same, when repeated between 29-32 weeks, had sensitivity and specificity of 100% and 100% respectively when the criterion was set as ≤ 2975 pg/ml.

Receiver Operator Characteristic curve for salivary progesterone and preterm labor

Figure 1

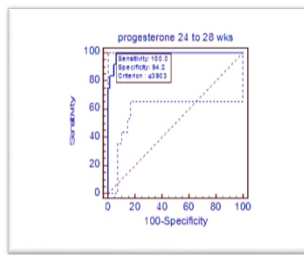
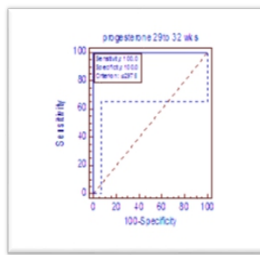


Figure 2



Similarly, sensitivity and specificity of transvaginal cervical length, in predicting preterm labor was 91.7% and 95.7% respectively at 24-28 weeks with the criterion was set as $\leq 3.1\text{cm}$ and 100% and 98.6% respectively, when repeated at 29-32 weeks, with the criterion set as $\leq 2.9\text{cm}$.

Receiver Operator Characteristic curve for transvaginal cervical length and preterm labor:

Figure 3

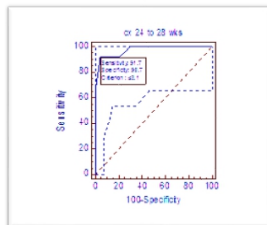
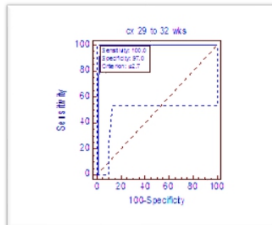


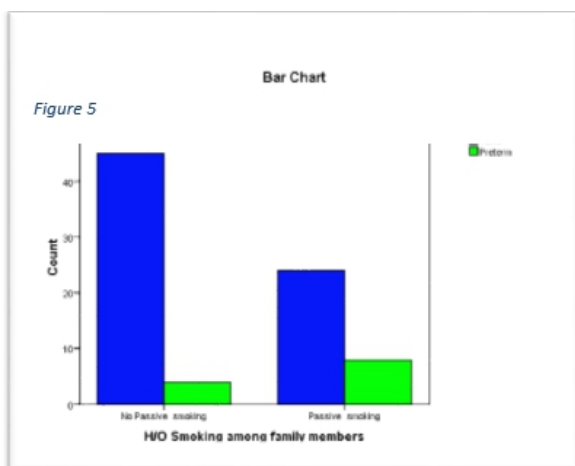
Figure 4



Age, BMI, socioeconomic status and working status were analyzed using chi square test and t-test. They did not have any impact on labor outcome and neonatal complications.

The relationship of passive smoking with preterm labor analyzed using chi square test had a P value of 0.037 which is significant. There is an increase in the incidence of preterm labor in the group with history of passive smoking. 66.7% in preterm group gave history of passive smoking whereas 34.8% in term group gave history of passive smoking. Figure

The relationship of NICU admission with respect to pregnancy outcome (term/preterm), analyzed using chi square test had a P value of 0.000 which is significant. Thus, neonates belonging to preterm birth group had higher incidence of NICU admissions i.e. 13.6% in preterm labor group vs 6.2% in term labor group. The relation of NICU admission with respect to neonatal complications analyzed using chi square test had a P value of 0.000 which is significant. The causes for NICU admissions were respiratory distress syndrome (99%), jaundice (4.9%), low birth weight (1.2%), skin infections (1.2%) and sepsis (1.2%). Incidence of neonatal mortality was 1.2% in the preterm group.



The t-test showed a good correlation between salivary progesterone and transvaginal cervical length with respect to pregnancy outcome and neonatal complications, with a P value of 0.000, which is significant. Lower the progesterone level, higher is the incidence of

preterm labor and neonatal complications.

The linear regression curve relating salivary progesterone level to gestational age at delivery, shows a statistically significant linear relationship. i.e., lower the salivary progesterone level, lesser is the gestational age at delivery. The regression equation thus derived i.e., multiplying the estimated salivary progesterone level by a constant value for that gestational age, at which salivary progesterone level is estimated, gives the gestational age of delivery.

$Y = 26.1645 + 0.002658 \times \text{Salivary progesterone level at 24 to 28 weeks.}$

$Y = 26.9582 + 0.002923 \times \text{Salivary progesterone level at 29 to 32 weeks.}$

Where Y is the gestational age at delivery.

Figure 6

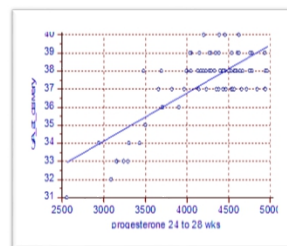
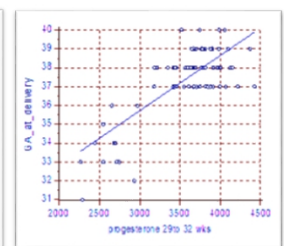


Figure 7



CONCLUSION:

Salivary progesterone is a better predictor of preterm labor when compared to transvaginal cervical length, as it has better sensitivity and specificity. It is a non-invasive method and sample collection is easier. Although transvaginal scan is available in every antenatal unit, it needs technical expertise and further, it shows inter-observer variability.

An ideal biochemical marker must be able to predict the problem at an earlier gestational age for appropriate interventions to be done. Hence, it is justified in doing the salivary progesterone estimation at 24-28 weeks though it has comparatively lesser sensitivity and specificity than at 29-32 weeks. In utero transfer can be advised for antenatal women whose salivary progesterone levels are $\leq 3903\text{pg/ml}$ at 24-28 weeks and $\leq 2975\text{pg/ml}$ at 29-32 weeks for better obstetric outcome and better neonatal salvageability.

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