Salivary Progesterone and Preterm Labor

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Abstract: Background: preterm labor is a major public health problem in loss of life and disability. The percentage of preterm labors has risen steadily over the last 2 decades salivary progesterone measurement may valuable in prospects of preterm labor. Objectives to study the benefit of salivary progesterone as an indicator of preterm labor **Patient and Methods**; this is a case controlled study has been carried out AL Zahra´a University Hospital during the period from 1st September 2011 to the 20 April 2012 and it was included 80 pregnant women from 26 to 34 weeks gestation. Those women were subdivided into 2 groups; 1st group (group A); 40 patients who have complained of warning signs of labor.2nd group (group B); 40 patients who were apparently healthy women not complaining of preterm labor. **Results**: Acceptable discriminative and predictive ability of salivary progesterone by ROC curve with sensitivity 85% and specificity 90% at cutoff rate 933.6 picogram /ml. **Summary and conclusion:** The salivary progesterone concentrations in the women with preterm labor were lower than those in control group. A cut off point 933.6 generated optimal sensitivity 85% and specificity 90% with diagnostic accuracy of 92%, so salivary progesterone level less than 933.6 pg\ ml is a predictor of preterm labor.

1. Introduction;

Preterm labor is known as the pregnant women showing contrations in the uterus with enough frequency and strength to cause vigorous effacement and dilatation of the cervical os before determined time of delivery (1).

It is a major cause of perinatal morbidity and mortality, and is estimated to account for 75% of neonatal mortality, excluding lethal malformations (2). It is not easy to determine the time of the preterm labor due to the preliminary symptoms and signs are usually weak and may take place during normal gestations. Therefore, several normal pregnant women will demonstrate symptoms through routine prenatal examination, where as other intended for preterm birth may discharge the early warning signs as normal in pregnancy (3).

Physiological, it is known that progesterone is necessary during the pregnancy for keeping the gestation and suppress the uterine contractions during gestational period. Where the presence of high level of progesterone helping in suppressing the uterine contractions and relaxation of uterine muscles via suppressing gap junctions, and decreasing the release and synthesis of prostaglandin, in addition to reducing in concentration of oxytocin receptors in the myoometrium and also, increase cellular calcium binding ability and has anti-inflammatory characters (4).

Salivary glands secrete the saliva which is considered as an ultrafilterate of blood plasma, and from between the body fluids, it is collection is non-intensive and can be collected at any time. For this reason, it is potentially valuable for measuring several parameters (5).

One of the substances which can be measured in the saliva is the progesterone hormone, where the level of progesterone in the saliva reflects the unbound, unconjugated biologically active fraction of the plasma hormone status. Estimation of progesterone in the saliva is easy to performed, beside it is not difficult to obtain and preserve the saliva for estimation of other parameters or hormones. There is marked in estradiol E3 concentrations and ratio of the estradiol to progesterone is more before term labor and in preterm delivery (6).

Assessing the salivary progesterone level is a non-invasive method with high sensitivity, its assessment between 20-30weeks of pregnancy is useful for predicting preterm birth. However, it must not be forgotten that preterm birth is amultifactorial process. None of the markers investigated for the prediction of preterm birth have adequate sensitivity or Specificity (7).

Aim of the work;

We aimed to diagnose preterm labor through the measurement of salivary progesterone.

2. Subjects and methods;

This is a case controlled study has been carried out AL Zahra´a University Hospital during the period from 1st September 2011tothe 20 April 2012 and it was included 80 pregnant women from 26 to 34 weeks gestation. Those women were subdivided into 2 groups;

1st group (patient group); 40 patient were complaining of warning signs of labor.

2nd group (control group); 40 patient who were apparently healthy women not complaining of preterm labor.

Inclusion criteria;

Single tone living pregnancy, between 26-34 gestational weeks.

Exclusion criteria

Evidence of fetal anomalies

Multiple pregnancies

Premature rupture of membrane

Pre- eclampsia, Placental abruption

Tocolytic therapy

All women subjected for full history taking, complete physical and abdominal examination, vaginal examination to assess cervical dilation and effacement and abdominal ultrasound.

Salivary collection;

Women were instructed to collect 2-3 ml of saliva between 8 clock AM and 8 PM o clock to avoid diurnal variation, the patient was instructed to wash the mouth with water and wait for 10 minutes than allow the saliva to run freely into slandered plastic jars then specimens were stored at -20c and kept until analysis.

Statistical methodology:

Data were analyzed using Statistical Program for Social Science (SPSS) version 17.

3. Results;

This study included 80 pregnant women, attended to Al-Zahra´a University Hospital, pregnant at 26-34wks gestational age are divided into two groups;

Patient group: 40 pregnant women of singleton pregnancy suffering from preterm labor. Control group: 20 pregnant women of singleton pregnancy with normal pregnancy.

Table 1. Comparison between patient and control group as regarded to maternal age

Age / year	Patient group	Control group	P value	sig
Range	18.0-35.0	20.0-34.0	0.401	N/S
Mean ±SD	27.300±4.821	26.450±4.151		

This table shows non significance difference between patient and control group as regards to the maternal age

Table 2. Comparison between patient and control group as regarded to salivary progesterone

Salivary progesterone	Patient group	Control group	P value	sig
Range	270.5-1100	618-1572.0	<0.001	H/S
Mean ±SD	729.2±223.3	1097.90±180.283		

This table shows high significance difference between patient and control group as regards to the salivary progesterone.

Table 3. Salivary progesterone levels in preterm patient group

Gestational age	Progesterone		ANOVA	
	Range	Mean ±SD	F	P value
30 w	270.5-867.0	601.60± 310.40	2.920	0.035
31 w	557.0-868.9	751.97±169.96		
32 w	629.4-1010.0	798.44±141.20		
33 w	541.0-1152.0	859.84±173.47		
32w	657.0-1100.0	889.68±140.05		

This table shows significant difference between gestational age in the patient group and salivary progesterone

Table 4. salivary progesterone levels in control group

Gestational age	Progesterone		ANOVA	
	Range	Mean ±SD	F	P value
31 w	947.0-979.8	963.40±23.19	0.820	0.492
32 w	881.6-1170.0	1049.49±101.38		
33 w	754.0-1216.0	1061.22±129.65		
32w	618.1-1572.0	1124.06±233.10		

This table shows non significance difference between gestational age in the control group and salivary progesterone

Table 5; correlation coefficient between salivary progesterone and other items;

parameter	Salivary progesterone		
	R	P value	Significance
Maternal age	0.058	0.721	NS
Gestational age	0.269	0.093	HS
parity	-0.026	0.873	NS

This table shows no important association among progesterone in the saliva with maternal parity and age but there is high significant correlation between salivary progesterone and gestational age

Table 6; ROC curve between patient and control group according to salivary progesterone level;

Cut off	Sens.	Spec.	PPV	NPV	Accuracy
≤ 933.6	85.0	90.0	98.5	85.7	0.921

Acceptable discriminative and predictive ability of salivary progesterone by ROC curve with sensitivity 85% and specificity 90% at cutoff rate 933.6 picogram /ml.

4. Discussion:

It is well known that prematurity or preterm labor is the main direct origin of early neonatal mortality accountable for about 27% or around 1 million mortalities annually (8) and also to highly significant morbidities in the newly born infants. Premature infants usually complaining from instability of body temperature, infections, hypoglycemia, respiratory distress, seizures, apnea, kernicterus, jaundice, necrotizing enterocolities, feeding difficulties, periventricular leucomalcia and hospitalizations Compared to infant born at term, preterm infants in comparison with full term labor infants (9).

Parity is defined as the number of preceding pregnancies with more than 28 weeks of gestational age. The subject of parity and the risk of pregnancy outcomes had been notorious for several decades (10). Parity is also known as a risk factor for premature births, and it has been anticipated that physiologic risk factors in multipara (e.g. postpartum hemorrhage, retained placenta and placenta previa) may somewhat clarify the higher risk of premature labor (11).

In this study there shows no significant linke between progesterone concentration in the saliva with maternal parity and age. This in agree with **Aliyu et al. (2005)** who demonstrating no significant association between increased parity and preterm birth. This also in agreement with **Eduardo et al. (2007);** who stated that there is no correlation between maternal age and salivary progesterone levels.

In contrast to **Chan et al. (2008)** who found that obstetric outcomes in women their ages 40 years or more was affected by Cesarean delivery, parity, and premature labor (before 37 weeks). Premature labor was alone connected with older age more than of parity. Therefore, the woman pregnant at older age is considered at a risk factor of premature labor.

The results of our study have shown that the salivary progesterone concentrations are rising up with the increase of the pregnancy duration (gestational age) in both groups. Our results disagree with **Gullman et al (2005)** who proposed that there were no significant changes in the serum progesterone levels or progesterone receptors before delivery.

Our study shows high significance difference between patient and control group as regards to the salivary progesterone. And this agree with **Priya et al (2013)** who found that salivary progesterone levels was significantly lower in all preterm women compared to the control. And **Lachelin et al (2009)** concluded from his work that the of salivary progesterone concentration between 28 and 34 weeks gestation was found to be significant lesser in women who went into normal delivery and delivered before

34 weeks of pregnancy than those with no symptom of labor (control group).

Our results revealed acceptable discriminative and predictive ability of salivary progesterone by ROC curve with sensitivity 85% and specificity 90% at cutoff rate 933.6 picogram /ml.

Summary and conclusions

The salivary progesterone concentrations in the women with preterm labor were lower than those in control group.

There was positive correlation between salivary progesterone and gestational age.

A cut off point 933.6generated optimal sensitivity 85% and specificity 90% with diagnostic accuracy of 92%so salivary progesterone level less than 933.6 pg\ ml is a predictor of preterm labor, so we concluded that we may be can use salivary progesterone as noninvasive biological marker for detection of preterm labor.

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