Research Article

Salivary progesterone as predictors of spontaneous preterm birth in comparism with cervical length

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Abstract

Background: Preterm labour still one of important causes of neonatal mortality and morbidity. Many researches on preterm labor were conducted in order to decrease the incidence, prevent complications, and improve survival rate for infants.
Objective: To assess if salivary progesterone can be used sa a predictive marker for preterm labour and to compared it to the use of cervical length measurement.
Study design: This Prospective observational study
Setting: The study was performed at AL-Yarmouk Teaching Hospital at the Department of Obstetrics and Gynecology (Baghdad – Iraq) for the period from February 2015 to February 2016
Patients and methods: The study involved 60 pregnant women between 28 weeks-34weeks gestation were divided into two groups; group A 30 patients with uterine contraction or history of previous preterm .group B 30 patient as control, cervical length of all patients was measured by transvaginal ultrasound ,saliva sample(washings) also collected and the level of progesterone in the saliva was measured by ELISA and the results were compared.
Results: statistical analysis of data showed that there was a significant relationship between salivary progesterone levels and preterm birth Sensitivity, specificity , predictive values (positive and negative) of progesterone were 96.7,90.0,90.6,96.4 respectively
Conclusion: salivary progesterone can be used as a predictor of preterm delivery in high risk group.

Key words: preterm, salivary progesterone

INTRODUCTION

Prematurity is one of major causes of neonatal death,[1] and serious morbidity such asneurodevelopmental problems, bronchopulmonary dysplasia intraventricular hemorrhage and cognitive difficulties.[2]

Preterm is delivery of baby after 20weeks and less than 37 week, The incidence of preterm birth 10 -12.5% of all births.[3] about one quarter of preterm births due to elective termination due to preeclampsia and IUGR[4] survivals rate was improved over the last two decades because of the introduction of surfactant, improvement of neonatal cares, and using of steroids.[5]

There are many risk factors of preterm labour some of these factors are modifiable other are not, these factors include age (<18,35>),multiple pregnancy, infection ,previous preterm labour, cervical incompetence, congenital abnormalities of uterus.[6,7]

Infants of African American mothers are 50% more likely to be born preterm than are infants of white mothers, so ethnicity plays a role.[8] Certain lifestyle and environmental factors, including: Smoking, alcohol ,drugs ,domestic violence ,exposure to certain environmental pollutants may be involved.[9]

Progesterone is steroid hormone produced by the adrenals, gonads, nervous system, and placenta in pregnancy it is a derivative of cholesterol.[10]

Its play important role in maintenance of pregnancy by blocking myomatrial contractility and therefore the onset of labour requires withdrawal of progesterone.[11]

Currently, different methods are used to identify which patient more vulnerable to preterm delivery depend on the risk factors & certain markers such as HCG, fibronectin, cervical length, However, none of these methods is known to be an accurate predictor of preterm delivery.[12]

PATIENTS AND METHODS

This prospective observational study performed in the department of obstetrics and gynecology of AL-Yarmouk teaching hospital (Baghdad – Iraq) from February 2015 to February 2016. verbal consent was obtained from all patients enrolled in the study .

60 pregnant women were involved at gestational age between 28 -3٤weeks with a viable singleton fetus. Week of gestation (GA) calculated from last menstrual period &early ultrasound. Exclusion criteria included: pregnant women with medical disease like hypertension, patients on steroids and progestional agent, if membranes was ruptured &mouth problems like bleeding gums, infection. fetalcongenital anomalies, intra- uterine growth restriction or antepartum haemorraghe not involved in the study. Patients divided into group A included 30pregnat women with abdominal pain due to contractions or history of preterm labour in previous deliveries or abortion in second trimester and group B included 30 healthy pregnant women were taken as control group.detailed history was taken.including (demographic data, past obesteric history,medical ,surgical ,drug and social history), general examination including vital signs and BMI were measured , abdominal and speculum examinations for assessment of cervix were done. Transavaginal ultrasound by ultrasounds department in hospital done for all the patients for measurement of cervical length (length<25mm was considered short), sample collection was done by ask the patient to rinse the mouth with water, and keep the water till 10min and then make saliva run into plastic cup, samples were refrigerated after collection within 30min at or below –20 C within 4h of collection. sample not collected if patient eat meal befor one hour .Level of progesterone was detected by ELISA

RESULTS

This study involved 60 pregnant women at gestational age between 28 -3٤weeks were divided into two groups, group A cases with preterm labour , group B was a normal pregnant women as control. Table 1 showed Main characteristics of the included women.

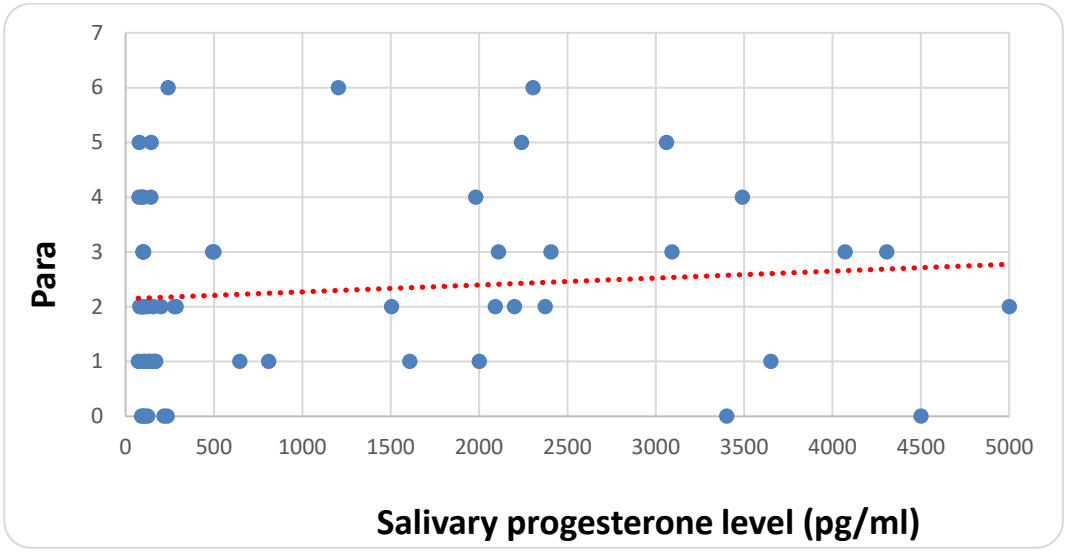
Table 1: Demographic distribution of data between studying group

Variables	Group I Mean ± SD	Group II Mean ± SD	p value
Age (years)	28.1±6.8	32.6±7.3	**0.015***
Gravida	3.6±1.9	4.6±2.2	0.075 (ns)
Para	1.8±1.4	2.8±1.7	**0.013***
Abortion	0.9±0.9	0.9±1.1	0.964 (ns)
Gestational age (weeks)	31.8±2	31.2±1.8	0.242 (ns)
Salivary progesterone level (pg/ml)	125.1±49.8	2064.9±1436.3	**<0.001***
Cervical length (mm)	23.2±2.6	17.6±12.9	**0.025***
SD= Standard deviation, *Significant at 0.05 level by independent t-test, ns= not significant			

Table 2 show level of salivary progesterone between studying group of Range (99.9-166.93) when gestational age less than 30 week in group A while its (76.67-3490.12)in the same gestational age in group B;and the level was ranging from 80.9 to 234.3 when gestatinal age more than 30 weeks in group A.

Table 2. : The level of progesterone in saliva of patients

		Salivary progesterone level (pg/ml)		ANOVA	
	Gestational age	**Range**	**Mean ± SD**	**F**	**p value**
Group I	<=30 weeks	(99.9-166.93)	116.5±23.5	1.182	0.343
	31 weeks	(80.9-98.9)	91.8±8.2		
	32 weeks	(80.5-275.96)	153.3±74.3		
	33 weeks	(71.43-142.2)	114.4±29		
	34 weeks	(76.53-234.3)	137.5±65.1		
Group II	<=30 weeks	(75.67-3490.12)	2030.8±1229.3	0.283	0.886
	31 weeks	(284.55-4307)	2516±1354.2		
	32 weeks	(143.39-5000)	1906.6±2262.7		
	33 weeks	(168.38-4500.07)	1969.9±1450.1		
	34 weeks	(645.2-2090.55)	1367.9±1022		



"Figure 1. The correlation coefficient between progesterone and paraity."

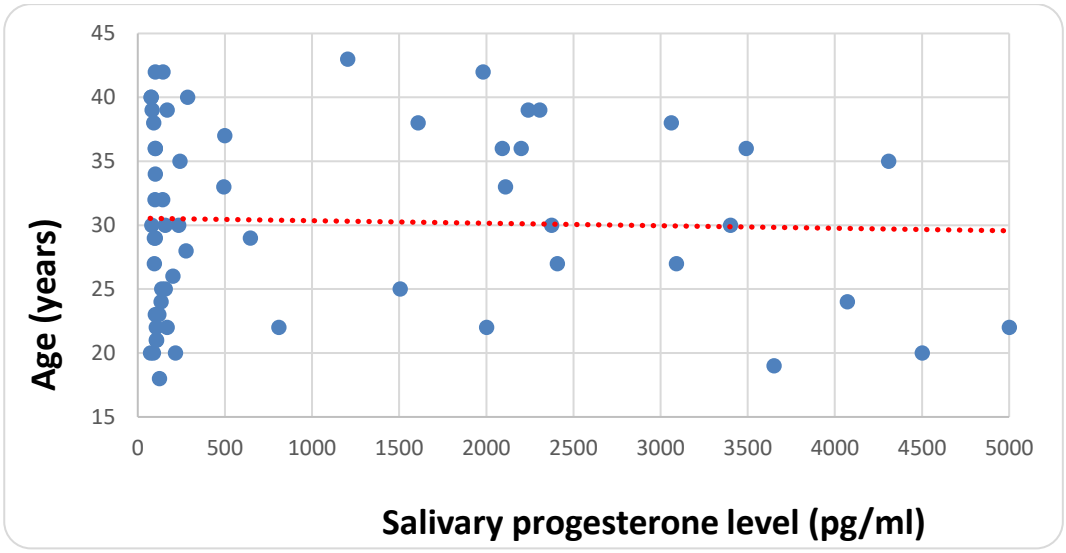


Figure 2. The correlation coefficient between progesterone and age.

Table 3. Sensitivity, specificity and accuracy and predictive value of predictors.

	Cut off (<=)	Sensitivity	Specificity	PPV	NPV	Accuracy
Salivary progesterone level (pg/ml)	**234.3**	96.7	90.0	90.6	96.4	93.3
Cervical length (mm)	**26**	93.3	56.7	68.3	89.5	75.0
Overall		100	90	93.8	98.5	93.9

Table 3 shows that measurement of salivary progesterone can predict preterm labour with 96.7% sensitivity and 90%specifity , cut off value was 234.3 pg/dl

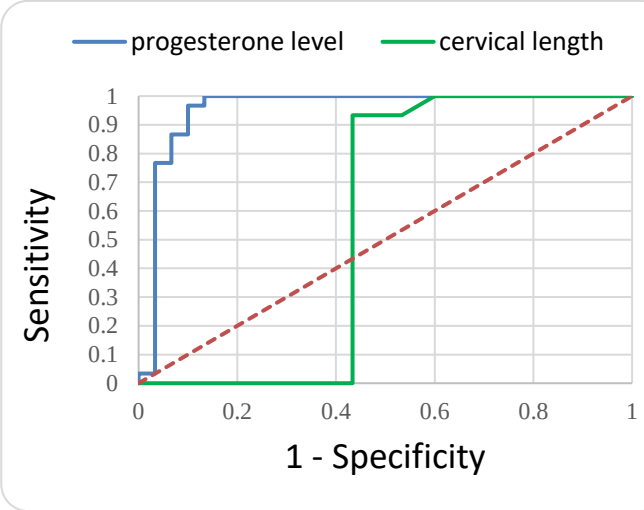


Figure 3 Receiver operation curve (ROC)of salivary progesterone & length of cervix.

Figure3 show both progesterone and cervical length had good predictive ability among studying group.

Figure 4 showed that there is inverse relationship between progesterone and cervical length as pregnancy advance,while Figure 5 A line regression showing significant inverse correlation between the cervical length and progesterone level p < 0.00.

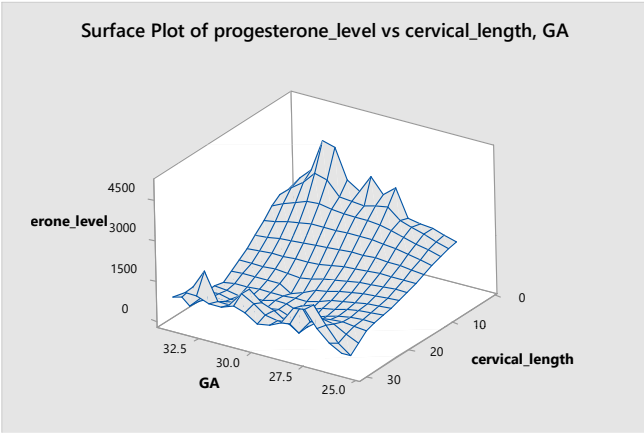


Figure 4:the relationship between progesterone and cervical length as pregnancy advance

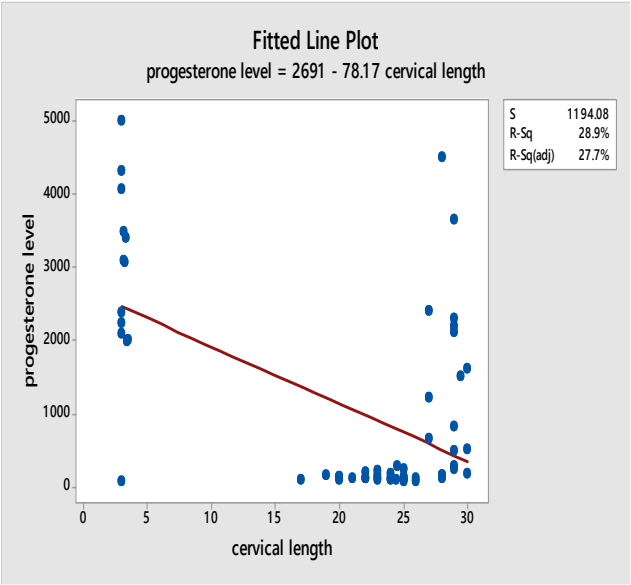


Figure 5 :A line regression between the cervical length and progesterone level p < 0.00

Statistical analysis

The data were analyzed using MedCalc ver. 12.5 Software.

- The continuous data presented as mean and standard deviation.
- Independent t-test (two tailed) was used for comparing them between study groups.
- The categorical data represented by frequency and percentage tables.
- Pearson's correlation was used to assess statistical relation between salivary protein and demographic data of women.
- Receiver Operator (ROC) curves used to assess the sensitivity and specificity.

A level of p – value less than 0.05 was significant

DISCUSSION

"Preterm birth" is the major cause of adverse outcome for mother and infant in both developed and developing countries, Eighty-five percent of neonatal morbidity and mortality is a result of prematurity. Progesterone is essential for maintenance of pregnancy its stabilize the myometrium.

The current study showed a significantly higher difference of salivary progesterone in group A with (preterm labour) if compared with the control group (125.1±49.8 versus 2064.9±1436.3 respectively). Ahmed M. Maged et.al study conducted at 2014 in Egypt , it involved 240 patients, half of them with preterm labour where the level of salivary progesterone (31.3 ± 3.75 in study group versus 38.5 ± 1.3 in control)

so it is lower in preterm group and afinding agree with our study.[13]

The length of the cervix can be detected by manual digital exam, but its is subjective test , with high failure rate especially inpregnant women without symptoms and with no cervical dilitation, and differences between examiners so this methods cannot be standered.

Cervical length is one of predictor for the preterm labour ,shortening of cervix and presence of funneling in ultrasound can detect that, in the current study the ability of both salivary progesterone and the cervical length for detecting preterm labour was compared it showed (sensitivity96.7 versus 93.3 for cervical length). There are a few studies focused on the length of cervix from the first to the second trimester of pregnancy and their predictive ability to detect preterm labour, "Carvalho *et al*. "measured the length of cervix of 529 women both at first & second trimester and found that the shortening of the cervicx was much more in women who lastly delivered preterm (13.9 mm) versus women deliverd at term (3.4 mm) and study suggest it is good predictor of preterm delivery;[14] in the current study cervical length cutoff value was25mm for the purpouse of study and its show 68.3 positive predictive value for preterm delivery.

Lachelin GC et.al showed that low level of progesterone in saliva were associated with spontaneous preterm labour in high risk group in this study92 patient were involved 28 patient with spontaneous onset of preterm of labour, and 64 of them had term delivery. The level of progesterone in saliva was less in the 12 women delivering preterm than in those delivering after(34 - 37 weeks), (P = 0.007) or at term (P = 0.009).[15] The recent study the level of salivary progesterone in high risk patient was lower than low risk patients p value 0.343versus 0.886 .

Priya B et.al study involved 90 woman 38 patient of them were high risk for preterm labour The mean level of salivary progesterone was obviously less in all patients who delivered at preterm compared with those delivered at term .cut-off level for progesterone in saliva was 2575 pg/ml, more than 80% of women how delivered prematurely had level less than the cut off value , with" sensitivity", "specificity", and" positive and negative predictive values" of 83% (95% CI 58.6-96.4%), 86% (95% CI 75.9-93.1%), 60% (95% CI 38.6-78.8%) and 95% (95% CI 87.1-99.0%), respectively,[16] mean while current study show cut-off value of **234.3**pg/ml and with sensitivity & specificity of 96.7,90.0 respectively.

Conclusion: in a study of limited number of patients, we conclude that salivary progesterone can be used as a predictor of preterm labour

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