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Research Article

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Investigating Relationship between Saliva Estriol to Progesterone Ratio and Preterm Delivery

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ABSTRACT

Preterm delivery is a serious obstetrical problem and leading cause of perinatal mortality in the non–anomalous infant. Therefore, the suitable screen test to determine high risk women is necessary. Salivary estriol to progesterone ratio changes during parturition. Therefore, using non-invasive, non-stress, and easy assessment of salivary estriol to progesterone ratio can be a reliable test for predicting preterm delivery. The present study aimed to investigate relationship between salivary estriol to progesterone ratio and preterm delivery. This was an analytical case –control study conducted on 76 women at 28-34 weeks of pregnancy referred to Ahvaz Imam Hospital in 2009. The saliva samples of 38 women with preterm labor symptoms and 42 women with normal pregnancy between 9 am-8 pm were collected and frozen at -20 ºC. Then, the salivary estriol to progesterone ratios were measured using Eliza method. The data were analyzed with SPSS version 18 using paired T test and Chi-square tests. The results showed significant difference in the mean estriol (p= 0.01), progesterone (p= 0.001), and estriol to progesterone ratio between the two groups (p= 0.001). Our findings showed that salivary estriol to progesterone ratio increased in preterm delivery; thus, it can be a good predictor of preterm delivery.

Keywords: Progesterone, Estriol to progesterone ratio, Saliva, Preterm delivery

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INTRODUCTION

Preterm birth for centuries has been an important cause of morbidity and mortality of fetus and a threat of neonatal health (1). Despite improvements in prenatal care and improved health indices and the extensive use of inhibiting drugs, preterm birth and death due to it during recent decades have not decreased (2, 3). Preterm birth accounts for around 70% of deaths in infants without defects, and about 50% of this total mortality is for infants who are born before 34 pregnancy trail. In 1999, for the first time, preterm birth was introduced as the greatest cause of infant deaths in developed countries. Moreover, in 1998, more than 28,000 infants in the United States died, 66% of whose death was within 4 weeks of birth, and the reason of at least two-thirds of these early deaths was due to preterm delivery (4).

In the world, 13 million children are born prematurely each year, and based on studies; its prevalence is 10-11 percent of total births (5). In the past 20 years, the incidence of premature birth in most developed countries is 7.5 percent of live births (6, 7). Overall, the incidence of preterm delivery in Iran is 12 percent (8).

Premature birth may be due to infection in any organ that activates inflammatory mediators and the secretion of prostaglandins, which initiate the uterine activity. Prevalence of these infections as a cause of preterm labor between 24 and 28 weeks of pregnancy is 70%, in 28 to 32, it is 40% and in weeks 32 to 36, it is 16% (9, 10).

Some scholars have pointed out a number of genital infections as the cause of preterm delivery. Koch et al. (1997) found that in women infected with trichomoniasis, the risk of low birth weight of newborns and the risk of preterm delivery increase (11).

The possible role of estriol and progesterone in childbirth, similar biochemical changes in on-time delivery with preterm labor, transfer of steroid hormones from the blood to saliva, and stress-free, non-invasive and easy nature of collecting saliva all lead to setting the minds toward the evaluation of the two hormones in saliva as a reliable test for the diagnosis of preterm labor.

Moreover, studying saliva does not need separation stage that exists in serum and can directly be used. Since estriol and progesterone have infinitely short half-life in plasma and their propagation to saliva occurs very fast, it can be a quick measure to predict preterm birth (12).

There is a normal increase in the average ratio of estriol to progesterone in saliva of pregnant women who give birth spontaneously after 42 weeks, whereas there was no increase in women who have need for labor induction at 42 weeks (13). In the research conducted by Hermann, estriol to progesterone increase starts at five weeks before calving begins and continues until birth (14).

Lachlin et al. showed that the proportion of estriol to progesterone in saliva increases from 18th week of pregnancy and increases rapidly in the last 5 weeks of pregnancy. The concentration of this increase is from less than 1 to more than 1 per person before calving (15).

Given that estriol in Iran saliva assessment is done just to predict preterm delivery and as no acceptable results were found, the researcher decided to conduct a study to investigate the relationship of estriol to progesterone ration in saliva with preterm labor, so as to suggest a test that is fruitful and has great predictive value and sensitivity.

MATERIALS AND METHODS

This study is a cross-sectional epidemiological study. This research was done after obtaining accreditation from the Medical University of Ahvaz. Inclusion criteria included age between 18 and 35 years, ultrasound in first trimester of pregnancy, and the exact age of pregnancy from first day of the last menstrual with regular menstrual, care during pregnancy (at least 3 times), single pregnancy and alive fetus.

The case group included 38 pregnant women of 28 to 34 weeks eligible to be studied who had referred to Imam Khomeini Hospital due to signs of premature labor. After taking history from the samples, vaginal examinations were carried out. Diagnostic criteria for start of labor were lasting uterine contractions with frequency of 4 in 20 mins or 8 per 60 mins with one or more other criteria including cervical dilation for 2 cm or more, 80% effacement or more and progressive changes in the cervix.

The control group consisted of 80 eligible pregnant women of 28 to 34 weeks who had referred to Imam Khomeini Hospital for pregnancy care. The process was explained to both groups and after obtaining written consent, their questionnaire forms were completed.

The patients were asked not to eat, drink, and rinse mouth at about an hour before sampling, and then at about 10 mins before sampling, they were asked to wash their mouth with water and after 10 mins, they were asked to pour 3 cc of their saliva gently in test tube.

In order to avoid circadian of hormones, sampling was done from 9 AM to 8 PM. The samples remained frozen until the end of sampling and finally were measured through ELISA test by estriol and progesterone kits, ELISA kits for this experiment were provided by Kavoshyar Company.

In the control group, those who referred for routine pregnancy care received training in theory form by the researcher on the initiation of uterine contractions associated with progressive pain, vaginal blood discharge, vaginal watery discharge, feeling of pressure in the pelvis. In each care, people were checked for preterm labor symptoms and in case of controlling preterm labor, people were trained similar to the control group.

Case group was followed up to delivery and birth date was recorded for each patient, and the control group members informed the researcher of delivery time by telephone and by going to the hospital, the researcher followed them until their delivery.

After gathering and encryption, data was statistically analyzed using Spss17. In order to evaluate statistical indicators like mean, standard deviation, absolute and relative frequency of descriptive statistics and to assess the significance of differences between the groups, inferential statistics, Type I error rate of 5% were considered. For the quantitative variables, t test and for qualitative variables chi-square was used.

RESULTS

Table 1 shows the demographic characteristics of the two groups, the results do not indicate a significant difference between the two groups.

Table 1. Frequency and percentage of demographic profile of case and control groups

Groups		Case group		Control group		P-value
Variables studied		Frequency	Percent	Frequency	Percent	
Age of mother	18-23	17	56	18	56	0.14
	24-29	13	25	11	18	
	30-35	8	19	13	26	
Job	Housewife	28	78.5	32	82	0.58
	Employed	10	21.5	10	18	
Address	City	31	81	35	86.5	1
	Village	7	19	7	13.5	
Level of education	reading and writing	10	28	6	14.5	0.85
	Basic	13	33.5	16	38.5	
	Diploma	14	36.5	17	40	
	Collegiate	1	2	3	7	

Table 2 shows there is no significant difference between gestational age in both groups (p= 0.49). Chi-square test variables between in the two groups show no significant differences.

Table 2. Frequency distribution of the samples in the case and control groups

Variable	Case			Control		P-value
Groups studied	Frequency		Percent	Frequency	Percent	
Gestational age in weeks	28-30	11	21	15	46	0.49
	30-32	18	60	17	38	
	32-34	9	19	10	16	
Number of pregnancies	1-2	22	70	24	67	0.08
	3-5	16	30	18	33	
The number of births	0-2	30	82.5	35	86.5	0.06
	3-4	8	17.5	7	13.5	
The number of abortions	0	27	76	37	88.5	0.09
	1-2	11	24	5	11.5	
The number of dead children	0	38	100	38	90	0.09
	1	0	0	4	10	
Number of living children	0-2	22	70	30	78	0.1
	3-5	16	30	12	22	

Chi-square test showed no significant differences in respiratory rate (p= 0.11) the number of pulse (p= 0.85) and temperature (p= 0.11) between the two groups (Table 3).

Table 3. Distribution of frequency and percentage of subjects in respiratory rate, pulse rate, and temperature

Variable		Case		Control		P-value
Groups studied		Frequency	Percent	Frequency	Percent	
Number Breathing	14-16	37	98	42	100	0.11
	16>	1	2	0	0	
Total		38	100	42	100	
Mean ± SD		0.86 ± 15.5		0.89 ± 15.5		
Number of Pulse	60-100	38	100	42	100	0.85
	100>	0	0	0	0	
Total		38	100	42	100	
Mean ± SD		5.8 ± 79.2		5.5 ± 79.2		
Temperature	36-37.3	37	100	42	100	0.11
	>37.3	0	0	0	0	
Total		42	100	42	100	
Mean ± SD		0.62 ±36.2		0.64 ±36.2		

Independent t-test showed no significant differences between the two groups in gestational age (P< 0.001). The results of this table show that the mean salivary estriol in the case and control groups, respectively, are 0.41 and 0.20 ng/m. Independent t-test showed significant differences between the two groups (p< 0.001).

The results of this table show that the mean salivary progesterone in the case and control groups are respectively, 2.7 and 8.7 ng/m. Independent t-test showed significant differences between the two groups (p< 0.001).

The results of this table show that the average ratios of estriol in saliva progesterone in the case and control groups are, respectively 0.20 and 0.022. Independent t-test showed significant differences between the two groups in the average proportion of estriol to progesterone (p<0.001) (Table 4).

Table 4. Comparison of the indices between the two groups

	Groups	Case	Control	P-value
Gestational age	Mean	31.4	39.1	0.001 >
	Standard deviation	2.34	0.77	
Estriol	Mean	0.41	0.20	0.001 >
	Standard deviation	0.16	0.3	
Progesterone	Mean	2.7	8.7	0.001 >
	Standard deviation	1.6	2.02	
Estriol to progesterone ratio	Mean	0.20	0.027	0.001 >
	Standard deviation	0.16	0.022	

DISCUSSION

In this study, the estriol concentration in the case group that is patients with preterm labor between 28 and 34 weeks of pregnancy was the greater the control group, women with normal pregnancies at the same gestational age. Moreover, the people in the control group had on time delivery. McGregor et al. (1999) studied estriol in saliva of 241 women with pregnancy age from 22 to 26 weeks until delivery by RIA (16).

Of these, 61 patients had preterm delivery between 24 and 34 weeks, 180 had on time delivery. Average estriol in saliva of case group, who give birth between weeks 24 and 34 was 1.8 ng/m, and the average estriol in the control group, people who had gave birth at 24 to 34 weeks and had no signs of preterm delivery was 0.8 ng/m. T test showed a significant difference between the two groups (p<0.01) (16).

Therefore, this study is consistent with the study by McGregor. However, the reason of differences in estriol concentrations with his study may be due to individual differences, genetic and racial factors and differences in methods of measurement, because RIA test is accurate and measures lowest levels of hormone. In a study conducted by Tehranian, et al. (17) on 43 pregnant women in 24 to 34 weeks with preterm labor pain, the average levels of

estriol in the treatment and control groups, respectively, were 0.41 and 0.20 ng/m, and a significant difference in the concentration of estriol was observed between the two groups ($p< 0.001$)

Findings of our study are not consistent with the findings of the Tehranian's study which can be due to the fewer cases in Tehranian's study, compared to this study.

According to the findings, significant differences were observed between the two groups in the mean progesterone ($p< 0.001$).

Smith et al. (2009) in a prospective study showed that the level of progesterone in groups of between 28 and 34 weeks of gestation for preterm delivery was 4.7 ng/m and this level in normal pregnant women at the same gestational age was 5 ng/m, and concentration of progesterone had reduced by 30 percent ($p<0.001$).

The amount of progesterone in women who had preterm delivery compared to women who had on time pregnancy was less ($p< 0.05$) (18). Thus, Smith's study is consistent with current research.

Despite these findings, Wang et al. concluded that progesterone concentration during labor (9.5 ng/m) compared with pregnancy (59.5 ng/m) was the same ($p>0.05$) (19).

This study is not in line with current research and this may be due to different patterns of secretion of progesterone in different people.

According to the findings of this study, the estriol to progesterone ratio showed meaningful differences in the two groups ($p< 0.001$).

In a study by Lachelin et al., the average ratio of estriol to progesterone in preterm birth between weeks 24 and 34 of pregnancy was equal to 4.6, which was more than pregnancy at the same gestational age and showed significant differences between the two groups ($p= 0.04$) (15). This study is also in line with the results of the present study.

Moreover, Darne et al. concluded that estriol to progesterone ratio in individuals with preterm delivery with healthy water pack was higher than 1 that had increased compared with normal pregnant people with the same gestational age increased ($p<0.05$) (20).

Regarding the relationship between these two hormones with pregnancy, measuring estriol to progesterone ratio can be used as a convenient screening test to predict preterm delivery, particularly in patients with high-risk pregnancy to be able to distinguish people at risk from healthy ones and use preterm preventive measures for people at risk and stop unnecessary and sometimes highly morbid intervention measures in healthy people.

REFERENCES

[1] Al. AFe. Blood Magnesium Levels and Preterm Birth. Faculty of Medicine, Tehran University of Medical Sciences. September **2007**;65(7): 460- 34.
[2] Hallak M. Hypertension in pregnancy. *High risk pregnancy: management option.* **1999**:639-63.
[3] James DK, Steer PJ, Weiner CP, Gonik B. High risk pregnancy: management options-expert consult: *Elsevier Health Sciences*; **2010**.
[4] Paneth NS. The problem of low birth weight. *The future of children*. **1995**:19-34.
[5] MMWR. Inrenational notes update: Incidence of low bivth weight. Aug **1984**;33:429-60.
[6] Mbair G MDea. *Averys neanetology Li ppini coh.* **2005**(6th USA.
[7] Tucker J, McGuire W. Epidemiology of preterm birth. Risk. 2004;1037:52.
[8] C. He. general Hygiene. *Arjmand Publication.* **2008**;2:141-1400.
[9] Vidaeff AC, Ramin SM. From concept to practice: the recent history of preterm delivery prevention. Part I: cervical competence. *American journal of perinatology*. **2006**;23(1):3-13.
[10] Vidaeff AC, Ramin SM. From concept to practice: the recent history of preterm delivery prevention. Part II: Subclinical infection and hormonal effects. *American journal of perinatology.* **2006**;23(2):75-84.
[11] MacDanld ea. Obstetrics Williams translations doctor Bahram judge the world. Edit Roxanne lawyer and doctor Mansour around the property. Tehran Golban Publications. **2010**; The twenty-third edition, **2010**.

[12] Marek B, Kot T, Buntner B. [Usefulness of measuring the levels of estrogens and progesterone in the saliva during pregnancy]. *Ginekologia polska*. **1989**;60(5):291-4.
[13] Moran DJ, McGarrigle HH, Lachelin GC. Lack of normal increase in saliva estriol/progesterone ratio in women with labor induced at 42 weeks' gestation. *American journal of obstetrics and gynecology*. **1992**;167(6):1563-4.
[14] Hedriana HL, Munro CJ, Eby-Wilkens EM, Lasley BL. Changes in rates of salivary estriol increases before parturition at term. *American journal of obstetrics and gynecology*. **2001**;184(2):123-30.
[15] Lachelin G, McGarrigle H, Seed P, Briley A, Shennan A, Poston L. Low saliva progesterone concentrations are associated with spontaneous early preterm labour (before 34 weeks of gestation) in women at increased risk of preterm delivery. BJOG: *An International Journal of Obstetrics & Gynaecology*. **2009**;116(11):1515-9.
[16] McGregor JA, Jackson GM, Lachelin GC ,Goodwin TM, Artal R, Hastings C, et al. Salivary estriol as risk assessment for preterm labor: a prospective trial. *American journal of obstetrics and gynecology*. **1995**;173(4):1337-42.
[17] Tehranian NMSS. The level of salivary estriol predictor of preterm delivery. *Journal of Medical Sciences*. **2008**.
[18] Stamatelou F, Deligeoroglou E, Farmakides G, Creatsas G. Abnormal progesterone and corticotropin releasing hormone levels are associated with preterm labour. *Annals Academy of Medicine Singapore*. **2009**;38,11101
[19] Wang Q, Chen Z, Xu Y. [The relationship between onset of labour and concentration of hyaluronic acid and estradiol to progesterone ratio]. *Zhonghua fu chan ke za zhi*. **1996**;31(8):477-9.
[20] Darne J, McGarrigle H, Lachelin G. Increased saliva oestriol to progesterone ratio before preterm delivery: a possible predictor for preterm labor? *Br Med J (Clin Res Ed)*. **1987**;294(6567):270-2.