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Role of Cervical IL-6 and IL-8 Levels in Preterm Labor in Nulliparous Pregnant Women

Sholeh Shahgheibi, [1] Abdorrahim Afkhamzadeh,[2] Narjes Noori *[3]

1. Department of Obstetrics and Gynecology, Kurdistan University of Medical Sciences, Kurdistan, Iran
2. Department of Social Medicine, Digestion and Liver Research Center, Kurdistan University of Medical Sciences, Kurdistan, Iran
3. Department of Obstetrics and Gynecology, Kurdistan University of Medical Sciences, Kurdistan, Iran

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*Corresponding author at:
Department of Obstetrics and Gynecology, Kurdistan University of Medical Sciences, Kurdistan, Iran
E-mail:
nnoori1385@gmail.com

Abstract

***Background*:** Premature birth is a cause of prenatal mortality and covers 60-80% of deaths caused by the congenital defects. Despite eye-catching developments in medical sciences, premature birth statistics are still high and impose hefty costs on the society. Laboratory indexes such as IL-6 and IL-8 are used to predict the preterm delivery. In this study, the role of IL-6 and IL-8 of cervix in women with preterm labor and term delivery were compared .

***Materials and Methods*:** This case-control study was performed on 89 patients, 60 patients in control group and 29 patients in the study group, who had symptoms of preterm labor. Endocervical swab samples were collected from all patients in order to study IL-6 and IL-8 levels using ELISA technique. SPSS-15 statistical software was used for the analysis of data. T-test was used to assess different qualitative variables.

***Results*:** 78 patients (87.63%) and 11 patients (12.35%) had term and premature deliveries, respectively. The two groups had not significant difference in terms of weight and size. A significant statistical difference only in cervix IL-8 was observed between the two term and preterm groups after comparison of the mean variables.

***Conclusion*:** Cervico-vaginal level of IL-8 in premature deliveries is higher than term deliveries and it can be used to predict premature delivery.

Introduction

The premature delivery is determined by the onset of labor [pains] before 37th week of pregnancy which accounts for 40-75% of neonatal deaths and 60-80% of infant deaths [1]. Its prevalence rate in the United States is roughly 10 percent; the rate would be even higher in the developing countries [2]. Despite the recent developments in health cares and therapeutic and diagnostic methods, unfortunately, its emergence and incidence rates have not been reduced in the recent years [3]. Different reasons have been stated for the preterm labor such as premature rupture of membranes, pregnancy complications such as blood pressure, existence of myoma, cervical insufficiency, fetal abnormalities, and multiple pregnancies [4, 5].

The mechanism of infection-induced preterm labor is so that the microorganisms present in the vagina or cervix form a colony after extending upward on fetal membranes and then, the bacterial toxin and LPS cause production of cytokine in mononuclear phagocytes. These cytokines in turn cause the release of prostaglandins and consequently accelerate the premature labor [6].

Although premature evaluation methods special to predict premature delivery are very limited, some laboratory indexes such as CRP, leukocytes and fetal fibronectin have thus far been considered effective in cervical secretions between 24-36 weeks of pregnancy in prediction of preterm delivery. Thus, it can be used as a rather easy test in diagnosis of preterm delivery [7].

Particularly the relationship between the fetal fibronectin and premature delivery and it can be used as a relatively easy and available test to diagnose the premature delivery. Recently, several studies have been conducted on the predictive effect of laboratory indices such as interleukin 6 (IL-6) and interleukin 8 (IL-8) present in the cervical fluid which cause inflammation of amniotic fluid and its relation with premature delivery, some of which have produced different results.

This study was carried out and designed in Be'sat Hospital of Sanandaj to compare vaginal cervical biomarkers level (IL-8 and IL-6) in women who were in their 24-36 weeks of pregnancy and suffering from pains of preterm labor and term pregnant women.

Materials and Methods

In this prospective cohort study, conducted in 2009, all pregnant women in their first 24-36 weeks of pregnancy, referred to the Maternity Ward of Be'sat Hospital of Sanandaj, considered as subjects of the study, with the following conditions: age range: 18-40 years old, body mass index (BMI): 18-26, with normal pregnancy, with no history of systemic diseases, without abnormal uterine, intact water cyst, lack of bleeding, with cervical dilatation, at least one centimeter.

The pregnant women with the following criteria were excluded from the study: excessive uterine enlargement as a result of polyhydroamnious, mother's high blood

pressure, placenta previa and abruption, rupture of fetal membranes, consuming antibiotic within one week before referring to the hospital, history of smoking cigarette.

After performing necessary sampling evaluation measures and with due observance to the above mentioned criteria, 30 pregnant women were selected. Then, one of them was excluded from the study and the control group was selected randomly in order to reach two fold of the said group (i.e. 60 pregnant women). In both groups, a sample of endocervical secretions was collected by the sterile swab after the subjects were examined by an obstetrician resident. The sample secretion was sent to the Immunology Ward of Medical Faculty within only 1-2 hours in order to measure IL-6 and IL-8 using ELISA method.

The checklist was considered as data collection tool which included the following information: age of mother, weight, date of first day of last menstruation, symptoms of preterm labor, laboratory results, and finally pregnancy. The information was registered in the checklist. Ethical considerations were observed in all patients, so that after receiving their informed consent, the procedure was explained to them and any more cost was not imposed on the patient. Data recorded in the computer through SPSS-15 software and *t*-test was used to analyze the data.

Results

In this cohort study, the following results were obtained after analyzing the data: There was not any significant statistical difference in both groups in terms of weight, size, body mass index (BMI) (Table 1). Of total patients participated in this study, 32 patients (36%) were low-literate people who accounted for the highest number of participants in this study. Moreover, five pregnant women (5.61%) were illiterate who constituted the minimum number of women in this study. The hemoglobin level was not significantly different between the two groups and hemoglobin levels (anemia) less than 10 mg/d1 was reported in eight pregnant women (9%). Total control group stood at 60 patients and 18 patients of them gave birth to a child on time while 11 of them gave birth to a child as premature delivery.

Although IL-6 level was higher in premature delivery group, such difference was not significant in both groups. However, IL-8 was significant in premature birth group (Table 2). In the present study, level of sub-curve stood at 45.1 and 99.7 percent with regard to IL-6 and IL-8, respectively (Fig. 1).

Table 1. Comparison of mean and standard deviation of indicators in two study groups

	Preterm labor Mean±SD	Term labor Mean±SD	*p*-Value
Age(year)	3.8±22.3	2.65±22.7	0.6
Weight (kg)	10±63.9	9.8±63.2	0.7
Length (cm)	5.3±159.3	5±157.6	0.2
BMI	3.43±25.16	3.8±25.5	0.3
Hemoglobin (mg/dl)	1.43±12.34	1±12.7	0.4

Table 2. Comparison of mean and standard deviation of il-6 and il-8 in two study groups

	Preterm labor Mean±SD	Term labor Mean±SD	*p*-Value
IL-6	31.67±29.7	9.86±22.57	0.24
IL-8	83.41±441.6	62.7±180.5	0.0001

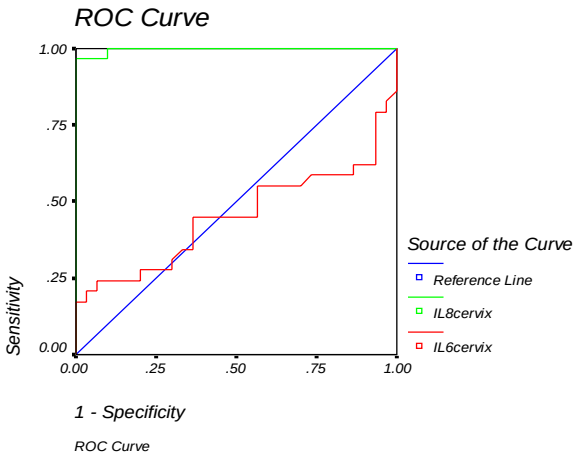

Figure 1. ROC Curve

Discussion

The present study is a case-control study which has compared IL-6 and IL-8 in the cervix of the primiparous mothers with preterm labor. In comparison of the average value of variables in both groups (case and control), IL-8 level in cervix of women with premature delivery was higher than that in women with term delivery, while the mentioned difference was not significant for IL-6. Interleukins are the cytokines which are released from leukocytes and other cells and can be distinguished from each other by a numerical suffix .

IL-6 and IL-8 are of mononuclear phagocyte cells which produce endothelial cells and fibroblasts and are activate in both innate and adaptive types. In the present study, interleukin level (IL-6) had not any significant difference in both groups while the results are not considered with past studies. Of course, cut-off point, as mentioned in these studies, varied from 1.4-16 ng/ml, which have an apparent difference with each other. This issue shows the necessity of fulfilling more researches with meticulous methodology.

For IL-8, the difference between the two groups was significant in the present study; this result was consistent with the studies made by Holst [14], Jacobson et al. [8], Gonzalez-Bosquet et al. [9], and Rizzo et al. [15]. That specific cut-off point has not been attained in the study of Gonzalez-Bosquet et al. and Jacobson et al [8, 9]. But in other studies, the value of cut-off point has been reported as large as 617 and 45 times for IL-8. Many studies suggest that women with higher risk of premature birth have higher interleukin levels than the women who have term of delivery but there is no consensus on the sensitivity and specificity of the IL. 50-100 percent sensitivity and its specificity have been varied between

67-87 percent and such difference is due to the cut-off point [15].

As it was stated, the relationship between IL-8 and the premature delivery in the present study and other similar studies has been verified, for IL-6, we could not find a relationship between this index and preterm delivery. Measurement of IL-8 in secretions of cervico-vaginal is valuable in the diagnosis of preterm labor and it can be benefitted. Although significant statistical difference was not observed between Il-6 concentrations in both groups, concentration of the cervical IL-8 was found more in women with preterm delivery.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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