Alteration in the phenotype of peripheral blood T lymphocyte in patients with idiopathic preterm labour

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Abstract

Objective: The current study aimed to detect some changes occurred on the surface of T lymphocytes manifested by CD3, CD4 and CD8 molecules that may have a role in patients with idiopathic preterm labour.

Setting: Al-Kadimyia Teaching Hospital / Department of Obstetrics & Gynecology for a period of one year (March 2002-March 2003).

Study design: Thirty patients with idiopathic preterm labour were enrolled in this study in addition to thirty healthy pregnant women as a control group. Blood samples were taken from both groups, lymphocytes were separated and immunofluorescent labeled by monoclonal antibodies to CD3, CD4 and CD8 surface markers.

Results: Patients have a significant low percentage of these surface markers in comparison with control subject.

Conclusion: The above findings confirm the suppression of cellular immunity in patients with idiopathic preterm labour.

Keywords: Preterm labour, Lymphocytes, CD3+, CD4+ and CD8+ cells

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Introduction

Preterm labour is the major cause of perinatal mortality and morbidity [(1)]. It is one of the most serious problems facing obstetrician and other perinatal health care [(2,3)]The basic function of immune system is to combat the numerous pathogens that are present in environment and the lymphocytes considered the key constituent of it. Only mature functional lymphocytes express a number of characteristic surface proteins and these CD-proteins are associated with T-cells receptor through non-covalent attachment.

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They serve to transmit signals from these receptors into cytoplasm and must be present for the receptor to be transported out of the cell surface. Almost exclusively T-lineage cells express the CD3 proteins and their presence is commonly used to identify T-cells in extrathymic tissues. The CD8 antigen is expressed on cells that have cytotoxic activity, these are extremely important in the defense against viral infection. The CD4 expressed on T-helper cells which promote proliferation, maturation and immune reaction of all other types of lymphocytes [(4)]. Mucosa of female genital tract is an immune barrier containing IgA secreting plasma cells, dendritic cells, and CD4+ and CD8+ T lymphocytes [(5)]. The uterus is not immunologically privileged site, it is well vascularized with good lymphatic drainage and can reject foreign tissue. Lymphatics are found in the uterus and cervix, some of which contain IgA, IgG, which is found to be increased in localized infection and unexplained

infertility, also CD4+ T lymphocytes and macrophage, are increased in cervical secretion in HIV infection [6]. High percentage of the decidual cells (75%) are composed of immune cells namely macrophage (20%), lymphocyte (10%), natural killer cells NK (45%) while the remaining 25% are stromal cells [7].

This study was conducted to see whether immunologic changes are present in patients with idiopathic preterm labour manifested by changing the percentage of certain surface molecules like CD3, CD4 and CD8.

Patients and methods

Cases were studied in Al-kadimyia Teaching Hospital and were divided into two groups, the patient's group (group A) includes thirty pregnant women with idiopathic preterm labour (PL) between 26 weeks and less than completed 37 weeks of pregnancy and was chosen depending on definition criteria. Other thirty healthy pregnant women with comparable gestational age were included as a control group (group B). The exclusion criteria includes patients with rupture membrane, chorioamnionitis, dead or compromised fetus, gross fetal congenital anomalies, multiple pregnancy, women with suggestive history of cervical incompetence and polyhydramnios. The gestational age was calculated from the first day of the last menstrual cycle and early ultrasonogtraphy. Patients enrolled in this study underwent general and obstetrical examination, routine investigations were done and they were observed and managed appropriately during labour. All newborns received by pediatrician and were admitted to the neonatal care unit for follow up. White blood cell (WBC) and differential count including lymphocyte percentage were calculated.

Sampling: five ml. of blood was collected from all women groups. Blood was collected with heparin. Lymphocytes separation was conducted according to Boyum; 1968[8] and Galun et al; 1994[9].

Regarding statistical analysis the results of CD markers were reported as percentage, mean, SD and SE. The significance was conducted using Student t-test and chi-square test was used in some comparisons.

Results

Total number of lymphocytes in peripheral blood for both groups showed no significant difference with P value = 0.761 as shown in (table 1).

Table 1: Total lymphocyte count in group A compared to group B

	No. Of patients	Mean	SD	SE
Group A	30	1727.03	832.9897	152.0824
Group B	30	1669.56	808.6800	147.6441

There was a significant decrease in the mean percentage of CD3+ cells in group A compared with group B with a P value < 0.00006 as shown in (table 2).

Table 2: CD3+ cells in group A compared to group B.

	No. Of patients	Mean	SD	SE
Group A	30	56.33	6.0591	1.1062
Group B	30	74.93	4.4947	0.8206

When we checked the percentage of CD4+ and CD8+ cells, results showed that these subset of T lymphocytes also significantly decreased in group A in comparison with group B with a P value ≤ 0.0000215 and ≤ 0.0000316 respectively as shown in (table 3) and (table 4).

Table 3: CD4+ cells in group A compared to group B

	No. Of patients	Mean	SD	SE
Group A	30	26.33	7.0238	1.2524
Group B	30	43.76	3.3496	0.6115

Table 4: CD8+ cells in group A compared to group B

	No. Of patients	Mean	SD	SE
Group A	30	5.73	2.5180	0.4597
Group B	30	17.10	1.6887	0.3083

(Table 5) shows a difference in the ratio of CD4+/CD8+ in both groups. The ratio was statistically significant with P value ≤ 0.0054.

Table 5: Ratio between CD4+ and CD8+ cells in group A compared to group B

	No. Of patients	Mean	SD	SE
Group A	30	4.59	2.7834	0.2750
Group B	30	2.55	1.98353	0.19834

Discussion

In 60 -70% of preterm labour, no identified cause was definite; we tried to determine if there is a role for immunologic changes in causing this state. The success of virtually all immune response depends on the remarkable ability of T cells, which accounts for about 75% of total peripheral lymphocytes [(10)]. T lymphocytes represented by CD3 positive marker found to be with a mean value of 74.9% in group B and a range of 70-80%. This result lie within normal value of T-cell which was consistent with what Branch-Dw who found that T cells is not appreciably altered during normal pregnancy [(11)], knowing that normal range of CD3+ in non pregnant individual is $0.9\text{-}2.8x10^9$/L which corresponds to 80% of total lymphocyte[(7)]. In contrast, CD3+ percentage was lower in group A with a mean value of 56.3% Which was statistically significant. This was in agreement with Oleszezuk et al[(12)]who found that CD3+ percentage decreases significantly in patients with idiopathic PL. Roughly 70% of T-cells in peripheral blood are CD4+CD8- and 20% are CD4-CD8+, while 5% are double positive CD4+CD8+. During normal pregnancy there is slight decrease in CD4+ (43.7% of total lymphocyte), which correspond to 63% of T-cells. In this study group A shows statistically significant lower level of CD4+ percentage with a mean value of 26.3% (equivalent to 46.7% of T-cells). This result was similar to what's found by Brandt et al [(13)], who suggest suppression in cell mediated immunity occurred in patients with preterm labour. CD8+cells constitute 20-25% of T cells, which constitute 18% of total lymphocyte [(14)]. In this study CD8+ found to be with a mean value of 5.73% in group A and a mean value of 17.1% in group B, this difference is significant with a P value of < 0.000316 and this is in agreement with (15&16) suggesting a suppressed cellular immunity in patients with idiopathic PL. The higher ratio of CD4+/CD8+ in group A compared with group B, this result reflects a suppression of the main two subsets of cellular immunity (helper & cytotoxic) in preterm labour patients.

From this study we concluded that an idiopathic preterm labour could be mediated through an alteration in immune system, which is represented by suppression of cellular immunity.

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