CYTOKINE PATTERN OF T_H1 AND T_H2 CELLS IN PREGNANCY

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Abstract - Experimental and clinical investigations indicate that antibody production and T-Helper 2 (T_H2) cytokine pattern, eg: Interleukine - 4, 10 (IL4, IL10) are dominant during pregnancy. Consequently, The T-Helper 1 (T_H1) cells activities decrease in pregnancy. Thus the cell- mediated immunity is partially depressed. All these events help fetus as an allograft survives in the mother's uterus. In this research we measured T_H cytokines in the sera of healthy pregnant and non-pregnant women (IL2, IL4, interfron-gamma; IFN-γ). Pregnant women showed significant decrease in mean serum level of IL2 and IFN - γ, this means depression of cell- mediated immunity. This finding explains increased incidence of some of the intracelluler infections and survival of the fetus during pregnancy.
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Key words: T-Helper cell, humoral immunity, cell-mediated immunity, cytokine, interleukine, interferon-gamma, pregnancy, infertility, abortion

INTRODUCTION

Pregnancy is a unique immunologic con lition that is accompained with changes in the im nune system (1 - 7). It is increasingly apparent that there is bidirectional interaction between the maternal immune system and the reproduc ive system during pregnancy (8 - 10). Recent stuc ies show that humoral immune responses are potentiated in the pregnant women, whi'e cell-mediated immunity is decreased during the normal pregnancy (1 - 7, 11 - 13). Recently researchers have focused on the role of T_H-cells subsets and cytokine pattern in pregnancy. Since T_H1 cytokines (IL2, IFN-γ) are generally harmful to maintenance of pregnancy, as a consequence the maternal immune system during pregnancy preferentially mounts T_H2- biased, resulting in increased susceptibility to certain autoimmune diseases and intracellular infections (1 - 4, 6, 12, 14 - 18).

There are also a number of infectious diseases caused by intracellular pathogens which appear exacerbated by pregnancy, e.g.: HIV associated infections, leprosy, coccidiomycosis, malaria toxoplasmosis and tuberculosis (1, 12, 19).

Increased incidence of some of intracellular infections and protection of fetus from T-cytotoxic cells' attack which is parallel with increase in humoral immunity rather than cell-mediated immunity, lead us to believe that cytokines production pattern has been changed.

While T_H1 activities adventure pregnancy, in order to prevent rejection of the fetus; T_H2 - type responses will be dominant, so, IL4, IL5 and IL10 productions increase especially in fetomaternal space. These cytokines are able to regulate production of T_H1 - type responses (1 - 4, 6, 12, 14, 15).

Studies have shown that cytokines, e.g.: IFN-γ and tumor necroziting factor-α (TNF-α) influence many of process of fertility and related to unexplained infertility as well as spontaneous / recurrent abortions (1, 5, 12, 16).

In the present research T_H1 and T_H2 cytokine pattern studied in healthy pregnant and non-pregnant women in order to elucidate the nature of the cytokines production pattern in pregnant and non pregnant persons.

MATERIALS AND METHODS

In present study serum samples were collected from 36 healthy pregnant women (in first and second trimester) in obstetrics clinic of Akbarabady hospital and from 30 healthy

non-pregnant women as the control group. Two groups ages were between 25 to 30 years old. Sera were separated from peripheral blood by centrifugation in the sterile condition and kept in -70°c until testing. We examined T_H1 and T_H2 activities by measuring their cytokine productions specially IL2, IL4; and IFN-γ as representation of their main functions. Determination of the cytokines level in each sample was accomplished using commercially available kits for each cytokine. Kits were based on micro-ELISA sandwich. The detail procedures was that of the manufacture's recommendations.

RESULTS

Results were statistically analysed using student's t-test. We found significant decrease in mean serum level of IL2 and IFN-γ in pregnant group.

Mean serum level of INF-γ and IL2 was 603.714 ± 137.97 *pg*/ml and 404.429 ± 232.039 *pg*/ml in pregnant group, respectively. While the serum level of the non - pregnant women was 834.5 ± 162.991 *pg*/ml and 838.668 ± 969. 923 *pg*/ml, respectively (Fig. 1) (Table 1).

Our results show that serum level of IL4 did not have any increase in non-pregnant women.

Table 1. Statistical analysis result of cytokines in normal pregnant and non - pregnant women

Sig. level	SD	Average	Number	IFN-γ (*pg*/ml)
	137.97	603.714	35	Pregnant
$1.47*10^{-7}$				
	162.991	834.5	30	non-pregnant
Sig. level	SD	Average	Number	IL-2(*pg*/ml)
	232.039	404.429	35	Pregnant
$9.37*10^{-4}$				
	969.923	838.667	30	non-pregnant
Sig. level	SD	Average	Number	IL-4(ng/ml)
	0.0698	0.149	35	Pregnant
0.07				
	0.0639	0.179	29	non-pregnant

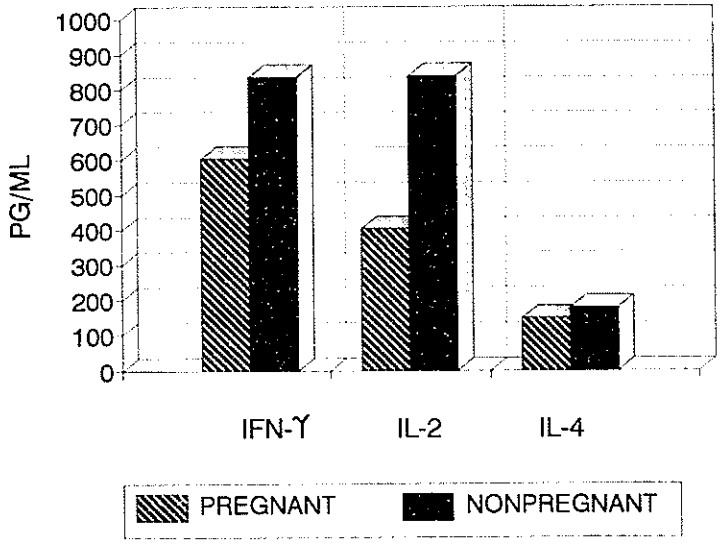

Fig. 1. Mean of IFN-γ IL2 and IL4 in normal pregnant and non-pregnant women.

DISCUSSION

We concluded that decrease in serum level of IL2 and IFN-γ in pregnant women may indicate the depression of cellular immuity and explain increased incidence of some of the intracellular infections and also autoimmune diseases seen during pregnancy. This might also explain survival of fetus which is an allograft within immuno competent mothers. Imbalance of T_H1, T_H2 cytokine pattern may be one of the immunologic causes in unexplained infertility and recurrent/ spontaneous abortions.

Therefore measuring of T_H1 and T_H2 cytokines in these cases will help to clarify immune pathogenesis of these abnormalities. If this is true, we might be able to prevent these immunological disorders by immunotherapy in the feature.

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