

Study on the Role of Interleukin-2 and Human Cytomegalovirus in Cases of Recurrent Spontaneous Abortion of Women in Wasit Province

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Abstract

Recurrent spontaneous abortions (RSA) is the loss of pregnancy for two consecutive times at least before the arrival of the fetus for 24 weeks gestation. This study was conducted to investigate the role of IL-2 and human cytomegalovirus in recurrent spontaneous abortions women in Wasit province. to conduct immunological studies and viral by 90 women who suffer from abortion frequently (At least two abortions) and two sets of control (pregnant and healthy women), The average age of the groups ranged between (17-45) years, the results showed a high significant increase ($P < 0.001$) at the level of IL-2 patients compared with pregnant women and healthy women, according to different age groups. And also it showed the results of a study of opposites immune IgM, IgG-virus human cytomegalovirus rise significantly ($P < 0.05$) for patients when compared with pregnant women and healthy women In the cases of chronic and acute infection .

Key words : *Recurrent spontaneous abortions (RSA) , Interlukin-2, CMV, IgM, IgG , Enzyme Linked Immunosorbent Assay (ELISA).*

Introduction

Recurrent spontaneous abortion (RSA) which known as repeated pregnancy loss ,it has no clear define at now Opinions differed about it, The American Reproductive Medicine Organization depend the tow pregnancy loss as (RSA) , While the European Organization of Embryology and Reproduction is considered three successive abortions and above as repeated spontaneous abortions⁽¹⁾. It is one of the most important and complications of pregnancy, especially in Iraq they have increased significantly in recent years, The causes are multiple, but most of the previous studies concentrate on parasitic and Viral causes⁽²⁾. Studies have shown a number of factors causing spontaneous abortion But the most common causes are immune disorders, Hormonal and metabolic disorders, anatomical uterine anomalies and infectious causes The most common are toxoplasmosis and cytomegalovirus However, more than 50% of the cases are still unclear⁽³⁾.

The role of interleukin 2

In general, about 5% of couples are believed to have recurrent spontaneous abortions which are

immunological reasons and increase this percentage may reach up to 40% after four losses of pregnancy⁽⁴⁾. The success of any pregnancy must be recognized and accepted by the mother's immune system Otherwise, it is considered as foreign and be expelled, Here comes the role of cytokines, which are low molecular weight proteins they are used to allow connections between cells⁽⁵⁾ They are particularly important in both innate and adaptive immune responses. For its central role in the immune system, Cytokines are involved in a variety of immune, inflammatory and infectious diseases. Its functions are not limited to the immune system, but it has a major role in many developmental processes during the stage of embryonic development and during pregnancy⁽⁶⁾ , Interleukin 2 is a monomer has 15.5 kD consisting of 133 amino acids, discovered more than 30 years ago in active T cells. It is mainly produced by cells (CD4-CD8-T) and a little produce it DCs and NK cell, IL-2 acts as a growth factor and promotes the proliferation and differentiation of natural killer cells to increase the normal functions of cells, It is also an effective stimulant for cell proliferation (T)If absent, T cells tend to go into hibernation or inactivity, It is therefore important to induce T cell proliferation and in maintaining both the regulatory and inflammatory role of T cells⁽⁷⁾.

The role of cytomegalovirus

The cytomegalovirus (CMV) came from the Greek word (cyto), meaning cell, and (megalo) large or overgrown. This is a viral genus from the group of human herpes viruses known as human herpes virus (HCMV) (8). It's one of the main causes of abortions and birth defects. Their clinical manifestations and symptoms in 90% of cases vary from severe fetal damage to death due to abortion (9). The prevalence of herpes virus (CMV) infection among women of childbearing age ranges from 35% to 95% in different countries, and increases with age (10). Cultural awareness as well as socio-economic status have a role in the spread of CMV infection and transmission (11). A recent study in Baghdad (12) indicates a high seroprevalence of cytomegalovirus in different age groups for men, women and children. The percentage was (68.78%) among the Iraqi patients and the rate of increase and rise compared to another study in Iraq as well was 57.2% (13).

Materials and Method

This study was conducted in the College of Science / Department of biology / Wasit University, In cooperation with Laboratories of Al Karama Teaching Hospital, Al Zahra Teaching Hospital, Al-Kut Hospital for Pedantries and Gynae obstetrics and some private clinics during the period from of 2019, The study included 90 women with recurrent spontaneous abortion and two control groups (pregnant and healthy) There were (60) women, (30) pregnant women and (30) healthy women who are not pregnant, The average age of the two groups ranged between (17-45) years. All information included: age, weight, height, housing, number of previous births, number of abortions and body mass index (BMI) value was calculated for all samples.

Interleukin-2

The work was done according to a company Cusabio Biotech is of Chinese origin, since this test uses Sandwich Enzyme Immunoassay.

Measuring the level of cytomegalovirus infection

We have been working in accordance with (14), detecting the presence of immunoglobulins (IgG / IgM) in the serum of both infected and two control groups, by using the ELISA method based on the principle of color change resulting from the binding of specific antibodies, Where (100 ml) from each diluted samples (Control

Samples) and control solutions (Controls groups sample) of each (NC –CC –PC), The additives are double for control solutions to ensure accurate results and are single for samples. then read in a short time not exceeding half an hour the results are recorded by the absorbance reading on along a wavelength (450 nm).

Statistical Analysis

Data were analyzed statistically using the program (Discovery Gen Stat) for statistical analysis of variance (ANOVA) was used, To find out the least significant difference (LSD) Comparisons were made between patients and control groups for the same age groups to find the significant differences between them was the least significant difference for the examinations studied below the probability level ($P < 0.05$) (15).

Results and Discussion

rate of changes in the level (interleukin 2) by Age Groups

The significant differences ($P < 0.001$) shown in Table (1) between the groups of aborted women and the control groups of pregnant and healthy, Interleukin 2 has been shown to play a major role in recurrent miscarriages and for all ages, it has also been shown to decrease its production during pregnancy as cytokines are originally regulatory immune proteins, It may affect some endocrine and placental activities and control the levels of secreted hormones, It also plays a major role in maintaining optimal conditions for fetal development and continuity of pregnancy or termination of pregnancy by abortion (16). Because it is categorized based on its inflammatory reactions to inflammatory cytokines and anti-inflammatory cytokines since inflammatory cytokines include interleukin 2, interferon IFN- γ and tumor necrosis factor (TNF- α), And its action in the cell are reactions delays hypersensitivity reactions it may also attack the fetus and trophoblast (17), So I found very high levels in our current study and for all age groups, The main act of increasing abortions is to increase the contractility of the uterine muscles by interleukin-2, as confirmed by a previous study (18). Therefore, the value of interleukin-2 for pregnant and normal women is much lower than abortifacients, This is proven by our study as the normal state is the balance between TH1 / TH2 cytokines, Turns towards the production of TH2 cytokines for successful and continuing pregnancy or tends to increase the production of inflammatory cytokines TH1, including interleukin 2, therefore,

pregnancy fails and ends with miscarriage or death of the fetus and this is confirmed by ^(19,20). the results of our current study are identical to a study in Iraq by ⁽²¹⁾.

Table (1) Rate of Changes in Level (IL₂) of Women with Repeated Abortions Compared to Control Groups by Age Groups

Age Parameters	Cases	1st. category (15-24 year)	2nd. category (25-34 year)	3 rd. category (35-44 year)	L.S.D
		Mean ± SD	Mean ± SD	Mean ± SD	
IL ₂ Pg/ml	Patients n= 90	A ±101.249.687	A ±109.511.03	A ±118.3 13.96	14.21
	pennants n=30	B 53.0± 11.06	B ±47.4 5.491	B ±56.9 5.727	
	Controls n=30	B ±44.7 5.960	B 12.18±57.5	B ±44.313.76	

*** Averages with different uppercase letters indicate a significant difference P <0.05 (vertical) for each criterion

Table (2): IgG and IgM infection rates for women with recurrent miscarriages by age groups

Age parameters	Cases	1st. category (15-24 year)	2nd. category (25-34 year)	3 rd. category (35-44 year)	L.S.D
		Mean ± SD	Mean ± SD	Mean ± SD	
CMV IgG mIU/L	Patients n=80+ve 2-ve	A 1.652 ± 0.365	A 1.682± 0.418	A 1.869 ±0.493	0.2683
	pregnant n=30+ve 0-ve	B 1.30 ±0.678	B 1.18 ± 0.545	B 1.352 ± 0.533	
	controls n=28+ve 2-ve	B 0.74 ± 0.330	B 1.063 ± 0.637	B 1.067 ± 0.501	
CMV IgM mIU/L	Patients n=42+ve 48-ve	A 0.951± 0.561	A 1.250 ± 0.629	A 1.660 ± 0.991	0.4428
	pregnant n=6+ve 24-ve	A 0.93 ± 0.476	A 0.930 ± 0.496	B 1.09 ± 0.399	
	Controls n=3+ve 27-ve	A 0.764 ± 0.419	B 0.551 ± 0.209	B 0.70 ± 0.481	

*** Averages with different uppercase letters indicate a significant difference P <0.05 (vertical) for each criterion.

*** CMV IgG Chronic infections of cytomegalovirus

*** CMV IgM Acute infections of cytomegalovirus

Influence of Cytomegalovirus Infection by Age Groups

The significant increase found in our study Table (2) in the case of chronic CMV IgG infection among women with miscarriage and control groups of pregnant and healthy and for all age groups, As well as acute infection CMV IgM where the result was a significant increase for the third category with pregnant women, and a significant increase for the second and third categories with healthy. Clear evidence of the prevalence of CMV infection for women in the province of Wasit. It is known according to recent statistics prevalence of CMV infections widely, especially among Iraqi women. The cytomegalovirus has a major role in repeated spontaneous abortions. Our study showed that the rate of chronic infection is higher than that of acute infection, these results corresponded to a study⁽²²⁾ in the province of Dhi Qar and also a study⁽²³⁾ in the province of Baghdad, In another study on abortifacients in Baghdad and the role of cytomegalovirus, seroprevalence of IgM from cytomegalovirus was the highest and most infections were in the first trimester of pregnancy, Given that pregnant women are the most affected category of viral infection, especially if the infection occurred during pregnancy, it either end the life of the fetus or be born deformed, So most studies have focused on the time of infection and infection in the first months of pregnancy is the most harmful. As the cytomegalovirus has the ability to alter the host's immune response, it changes the cellular nature of the placenta and weakens the immune mechanism of the fetus and its mother This leads to the life of the fetus⁽²⁴⁾, The results of the present study are consistent with^(25,26).

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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