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Study on anti-phospholipid syndrome and tumor necrosis factor in woman with recurrent spontaneous abortion in wasit province

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Abstract--Recurrent spontaneous abortion (RSA) is defined as the loss of pregnancy for at least two respectively times before the fetus reaches the twenty-four week of pregnancy, and its causes are multiple, some of which are known, but 50% of them are still unexplained. Antiphospholipid syndrome (APS), is one of the autoimmune diseases that can cause blood clots and lead to abortion or loss of the fetus in the first trimester of pregnancy. The study included 44 women who had repeated spontaneous abortions (two abortions or more) as well as two control groups (pregnant and healthy) who numbered 44 women, where 22 are naturally pregnant with a period of pregnancy 1-5 months without having had a previous abortion and 22 healthy women who are not pregnant and have given birth at least one child without previous abortions. Antiphospholipid syndrome was found to have a significant effect ($p \leq 0.05$) on abortion for aborted women to the control group (pregnant and healthy), as well as it was found that there was a significant rise ($p \leq 0.05$) in the level of tumor necrosis factor for abortions compared to pregnant women.

Keyword--Recurrent spontaneous abortion (RSA), Antiphospholipid syndrome (APS), Tumor Necrosis Factor (TNF).

Introduction

Recurrent pregnancy loss (RPL), defined as two or more respectively abortions, is attributable to multiple causes. However, in 50% of cases no known cause is

found. Although endometritis is a known cause of abortion, other inflammatory processes may play a role in idiopathic, recurrent loss [1]. The causes of recurrent loss are multiple, one of them is APS antiphospholipid syndrome it is an autoimmune disease in which the body attacks itself, as it manufactures antibodies that are proteins that attack phospholipids. Phospholipids are a type of fat found in all living cells and cell membranes, including blood cells and the lining of blood vessels.

The cause of the immune system's manufacturing of phospholipid antibodies remains unknown. Some people may have phospholipid antibodies in the bloodstream for a long period of time without causing any type of clot [2]. The main clinical features of APS phospholipid antibody syndrome are vascular thrombosis and frequent abortions in the 1960s. The pathogenic role of APS-phospholipid antibody syndrome in thrombosis growth has not been fully understood despite the strong association between APS and thrombosis. There are many pathogenic effects of APS, such as: thrombocytopenia, venous thrombosis, obstetrics and loss Recurrent pregnancy, stroke, transient ischemic attack, migraine headache, seizures, cognitive dysfunction, cardiac artery disease, skin manifestations, skin ulceration and necrosis, glomerulonephritis, renal thrombopathy and other aspects [3].

Tumor necrosis factor (TNF) was first identified in 1984 as cytokine with anti-tumor effects in vitro and in vivo. Extensive research since then has shown that there are at least 18 distinct members of the superior TNF family and that they account for 15% to 25% of the amino acid similarity with each other. The tumor necrosis factor weighs approximately 17 kD and is triangularly shaped. Family members are associated with distinct receptors, which are homogeneous in their extracellular domain. These cytokines have been involved in a wide range of diseases including tumors, viral reproduction, bone resorption, rheumatoid arthritis, diabetes, and other inflammatory diseases [4]. Excessive production of tumor necrosis factor causes malaria and internal toxins. Tumor necrosis factor (TNF) plays a major role in inflammatory and vascular processes after [5]. TNF inhibitors have been associated with thromboembolic events, they may prevent brain edema after stroke [6]. This cytokine was mainly produced by monostimulating cells, macrophages, and T-lymphocytes, and has been found to be elevated in patients with both, SLE and APS [7]. We hypothesized that TNF may be elevated in APS patients, with thrombosis as its prominent characteristic, more than those with other autoimmune diseases where autoimmunity prevails [8].

Materials and Methods

Blood samples were collected from hospitals and the central health laboratory in Wasit province during the period from December 2018 to May 2019. The study included 44 women with recurrent spontaneous abortion and two control groups (22 pregnant and 22 healthy women who are not pregnant). The average age of the two groups ranged between 17-45 years and all information including: age, weight, height, housing, joint pain, thrombosis, and hair loss, number of previous births, number of abortions, and body mass index (BMI) value was calculated for all samples.

Statistical Analysis

The data were statistically analyzed using the SPSS Statistic version 18 program for statistical analysis, where one way Anova was used to find out the least significant difference LSD, and Chi-square was used and comparisons were made between patients and two control groups for age groups The same and body mass index categories, for the purpose of knowing the moral differences between them, and the least significant difference for the tests studied was under the probability level ($P \leq 0.05$) [9]

Results

The significant differences ($P \leq 0.05$) shown in Table (1) between the groups of aborted women and the two control groups pregnant and healthy women showed that the APS syndrome has a significant role and is essential in cases of recurrent abortions and for all ages as it affects different age groups. Table (2) indicated a significant increase ($P \leq 0.05$) in phospholipid antibody syndrome levels for women with recurrent abortions. The above table indicated that there is a significant difference $P \leq 0.05$ between abortions and non-pregnant (control group) for APS phosphorous fat syndrome as it found that the syndrome levels are high in the category of abortions compared to non-pregnant women, and there is no significant difference between the different body mass index groups for each of the abortions and non-pregnant women.

The results showed in table(3) a significant increase in abortion ($P \leq 0.05$) in the level of tumor necrosis factor in the four groups, where the highest percentage was in the fourth category and followed by the first three groups compared with pregnant and healthy women.

Table (1) the rate of changes in the level of anti-phospholipid antibody syndrome (APS) for women with recurrent miscarriages compared to the two control groups by age groups.

Group study Age categories	Abortion $\mu\text{g/ml}$	pregnant $\mu\text{g/ml}$	Non pregnant $\mu\text{g/ml}$	P value	LSD
16-20	A,a33.153+ 4.394	A,b15.819+ 1.309	A,b16.184+3.063	0.0031	4.530
21-25	A,a29.911+ 3.851	A,b14.383+ 1.182	A,b17.035+0.872	0.0045	5.267
26-30	A,a33.568+ 6.769	A,b15.165+ 1.227	A,b16.518+2.528	0.0002 6	3.251
30>	A,a29.002+ 2.803	A,b16.274+ 1.797	A,b17.195+2.000	0.0012 1	3.164
P value	0.306	0.411	0.359		
LSD	Non.Signi.	Non.Signi.	Non.Signi.		

- Different capital letters indicate a significant difference $P \leq 0.05$ between different age groups.
- Different small letters indicate a significant difference $P \leq 0.05$ between groups.

Table (2) Rate of changes in the APS test for women with repeated miscarriages according to the Body Mass Index (BMI)

Group study BMI	Abortion µg/ml	Non pregnant µg/ml	P value	LSD
18.5-23	A,a28.847±2.177	A,b17.572±2.501	0.0015	3.519
23-27.5	A,a31.599 ±5.012	A,b16.289±1.658	0.00290	2.840
27.5>	A,a29.527±3.584	A,b16.997±2.713	0.0053	5.081
P value	0.117	0.226		
LSD	Non .Signi.	Non .Signi.		

• Different capital letters a significant difference $P \leq 0.05$ between groups according to the body mass index.

• Different small letters indicate a significant difference $P \leq 0.05$ between the groups studied.

Table (3) the rate of changes in the level of (TNF) for women with recurrent miscarriages compared to the two control groups by age groups

Group study Age categories	Abortion Pg/ml	Pregnant Pg/ml	Non pregnant Pg/ml	P value	LSD
16-20	AB,a99.14±21.10	A,b74.579±5.101	A,b78.13±7.05	0.0031	8.11
21-25	AB,a101.82±22.71	A,b77.547±4.199	A,b76.01±5.41	0.0016	5.92
26-30	B,a94.63±22.89	A,b76.187±3.346	A,c72.29±8.65	0.0052	6.29
<30	C,a111.68±22.49	A,b73.209±6.602	A,b75.67±21.7 9	0.0071 6	7.18
P value	0.0072	0.153	0.185		
LSD	7.46	Non.Sign.	Non.Sign.		

• Different capital letters indicate a significant difference $P \leq 0.05$ between different age groups.

• Different small letters indicate a significant difference $P \leq 0.05$ between different age groups.

Table (4): Rate of changes in the tumor necrosis factor (TNF) test for women with repeated miscarriages according to the body mass index (BMI)

BMI \ Group study	Abortion Pg/ml	Non pregnant Pg/ml	P value	LSD
18.5-23	A,a19.44+8.37	A,b77.61+8.30	0.0041	4.166
27.5-23	A,a18.87+9.73	A,b75.74+5.31	0.00025	6.289
>27.5	A,a18.85+8.06	A,b71.92+5.90	0.00290	6.280
P value	0.261	0.307		
LSD	Non.Sign.	Non.Sign.		

- Different capital letters a significant difference $P \leq 0.05$ between groups according to the body mass index.
- Different small letters indicate a significant difference $P \leq 0.05$ between the groups studied.

Table (4) indicated a significant increase ($P \leq 0.05$) for women who suffer from recurrent abortions. In our current study in the above table when comparing women with recurrent spontaneous abortions with the control group (not pregnant) and for all categories of body mass index, no significant effect of the level of tumor necrosis factor (TNF) was recorded between different BMI groups, so I found levels of tumor necrosis factor TNF is high in the small classes (18.5-23 kg/m²) and natural (23-27.5 kg/m²) and in the larger groups (more than 27.5 kg/m²) i.e. with overweight.

Discussion

Table (1) indicated a significant increase in the value of ABS. The syndrome is one of the autoimmune disorders that affects how blood clots, which leads to major problems in the body, and affects a large proportion of the female compared to male. It occurs when an antibody (proteins) present in the blood are impaired, and natural antibodies fight infection, but in the case of antibodies, the antibodies attack the fats that coagulate the blood, which leads to blood clots in abnormal proportions, and may sometimes cause seizures Heart, brain, or pulmonary embolism, and in some cases it may lead to abortion, rash, ulcers, and drops in platelet levels in the blood. The pregnancy loss associated with APS syndrome is usually attributed to thromboembolism in the uterus choroidal vessels different respectively [10].

In future untreated pregnancies, women with recurrent abortions and persistent positive tests For APS they have a possible abortion rate of up to 90%. It appears that these antibodies may not directly affect the early stages of embryonic implantation but rather affect the invasion of trophoblastic and placenta [11]. The results of our current study were identical to a study in Iraq by [12].

Table (2) indicated a significant increase ($P \leq 0.05$) in phospholipid antibody syndrome levels for women with recurrent abortions. Obesity during pregnancy is a major concern due to known risk factors for both the mother and the fetus, as complications in pregnancy include frequent abortions and gestational

diabetes. APS antibody syndrome for phosphorous fats and obesity are both chronic diseases that have similar long-term consequences for the mother during pregnancy. The situation worsens, such as arterial and aortic thrombosis and harmful obstetric outcomes such as frequent fetal loss, preeclampsia and intrauterine death of the fetus [13]. It may be partly equivalent to partially endurance in women with the gradual accumulation of fat [14].

Table (3) indicated a significant increase in abortion ($P \leq 0.05$) in the level of tumor necrosis factor in the four groups. In laboratory studies it has been claimed that TNF tumor factor protects the fetus from teratogenic effects [15]. That TNF tumor necrosis factor regulates the invasion characteristics of trophic aroma by regulating Matrix metalloproteinase 2 (MMP2) and Matrix metalloproteinase 9 (MMP9) [16]. On the other hand, an animal study found that TNF leads to loss of immune pregnancy [17]. Cytokines seem to play an important role in causing unexplained repeated pregnancy loss. Similar results were obtained in a study conducted by [18].

Table (4) indicated a significant increase ($P \leq 0.05$) for women who suffer from recurrent abortions (19). The high levels of this type of cytokines in abortions is the main and important factor in cases of repeated abortions as it is used to stimulate programmed cell death for trophoblastic cells [20]. Hence, it can be said that cytokines participate in the immune reaction of the mother and fetus and have an important role in determining the success of pregnancy. The results of our study were identical to that of [21].

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