World of Science: Journal on Modern Research Methodologies

Volume 2 Issue 12, Year 2023
ISSN: 2835-3072
https://univerpubl.com/index.php/woscience

Role of Cytomegalovirus Infection and Concentration of Free Radicals in Success Range in Women That Undergoes Intrauterine Insemination in Baghdad's Population Couples

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Article Information

Received: Oct 29, 2023

Accepted: Nov 30, 2023

Published: Dec 31, 2023

Keywords: *IUI; contaminated water; Cytomegalovirus; Pollution.*

ABSTRACT

The current study focused on the role of age, free radicals and presence of Cytomegalovirus infection among wives who underwent the process of artificial insemination (IUI) and also the increase in the proportion of free radicals in the blood plasma and its relationship with water and food pollution in the spread of the disease of CMV for the period from 1/11/2022 to 1/9/2023 in special laboratory for IUI procedure (AL- Amal)

This investigation included 60 women who underwent (IUI) program with positive results of IgG and IgM Cytomegalovirus infection and compared to 30 wives who tested negative result for the same infection as case control, for age groups from 20 to 35 years. The results indicated that there are high statistic levels in terms of infected and uninfected women (p <0.01) in the IUI programs.

Oxidative stress has been priginats a potential role in outcome of invitro fertilization (IUI) and Intracytoplasmic Sperm Injection ICSI). Our new research, all of wives that undergoing IUI programs, are in cases of female factor infertility. There are highly significant deference between low and high value of Malondialdehyde as marker of oxidative stress. (P<0.01).

***AIMS:** To define the correlation between age, oxidative stress and Cytomegalovirus infection with percent of IUI succeed by using Cytomegalovirus IgG and IgM test which they exposed to environmental pollution as water and food pollution.*

Introduction

Human Cytomegalovirus (CMV) infection has become common worldwide with a seropositivity rate of 40-100% in developing countries. This virus is belong to the family (Herpesviridae) and causes several health problems (1, 2). The primary infection of CMV causes loss in pregnancy, some explanations have been documented (3-5). A study has found a higher CMV antigen in the abortion tissue and higher seropositivity (6). Controversial findings have been seen in prospective studies. Some of them found a higher risk of pregnancy loss while others didn't prove it(7),(8). Some other studies observed a high prevalence and high titers antibody to CMV in recurrent abortion cases, while others found less prevalence of CMV antibodies in aborted

women than in healthy women.(9), (10).

Intrauterine insemination is an assistant reproductive technology (3). In general intrauterine insemination (IUI) should be the first choice in treatment of subfertility in men and women for unexplained cases, instead of entering in to expensive assisted reproduction techniques like IVF AND ECSI (11).

The basic idea behind intrauterine insemination (IUI) is to stimulate sperm by passing the cervical barrier and mucus and having a high percentage of natural forms at the fertilization positions (3). Also IUI may be the first stipe for curing male subfertility which caused by: aspermia, vaginismus, impotence, hostile cervical mucus and other abnormalities (12). IUI is a procedure that depend on preparation of washed motile spermatozoa, by which we can remove infection, leucocytes, prostaglandins, antigenic proteins, non-active motile sperms and other components like immature germ cells (13). This procedure increase the quality of the sperm by decreasing the percentage of formation a free radicals substances after sperm activation, by which improvement of fertilizing capacity of the spermatozoa (13). Other studies by New Zealand and other countries showed that about 80% of fertility centers are cost-effectiveness of IUI procedure, but about 35% of these fertility centers till now do IVF program as a first method for chose (14). The techniques are very simple to be performed, and the costs are very lower in comparison to the expensive Assist Reproductive Technology (IVF and ICSI) programs. Besides any severe complications after this method are very rare (15). Because of the cheep and safety simple program in with administration clomiphene citrate or natural cycle make it to be used also in developing countries (16). Oxidative stress is the state of being unbalanced between reactive oxygen species (ROS) and defense materials such as vitamin E and C. (17). Copper–zinc containing superoxide dismutase that contain Zinc and Copper (Cu, Zn-SOD), catalase, and other materials like GPXs (glutathione peroxidases), are the potent antioxidant defense against oxygen species that have properties of oxidizing the ROS substance (18).

In spite of significant advancing in (ARTs) programs, the succeeded rate of till not convincing (about 35%) (19). So that this serious substance (ROS) has been considered as effective important factors that control the outcome of IVF and ICSI procedures (20).

Environmental pollution and most type of diseases increase body free radicals, as well as some other factors like (e.g. nutrition, smoking and obesity) which play an important role in most pathologic processes like cancer, cardiovascular diseases, periodontitis and diabetes (21), (22). Previous studies have shown that, identification of oxidative stress biomarkers by sampling endometrial secretions and menstrual discharge (3).

Investigation by other researchers found that, implantation stage of the fetus and also early post implantation period is very sensitive for ART outcome, because ROS-induced oxidative damage of the implanted or non-implanted embryos. So that ROS can reduce developing organisms and negatively affect establishment of pregnancy (3). Repetitive abortion and idiopathic recurrent pregnancy loss are as result of adverse effects of oxidative (23). There are several evaluation method for detecting the endometrial maturity and receptivity to new embryo (24). In depend of recent studies found that endometrial secretion is important factors that affect the implantation of the embryo inside the intrauterine environment (25). Other studies suggested that cytokines such as IL-1β have significant role (IVF) (26).

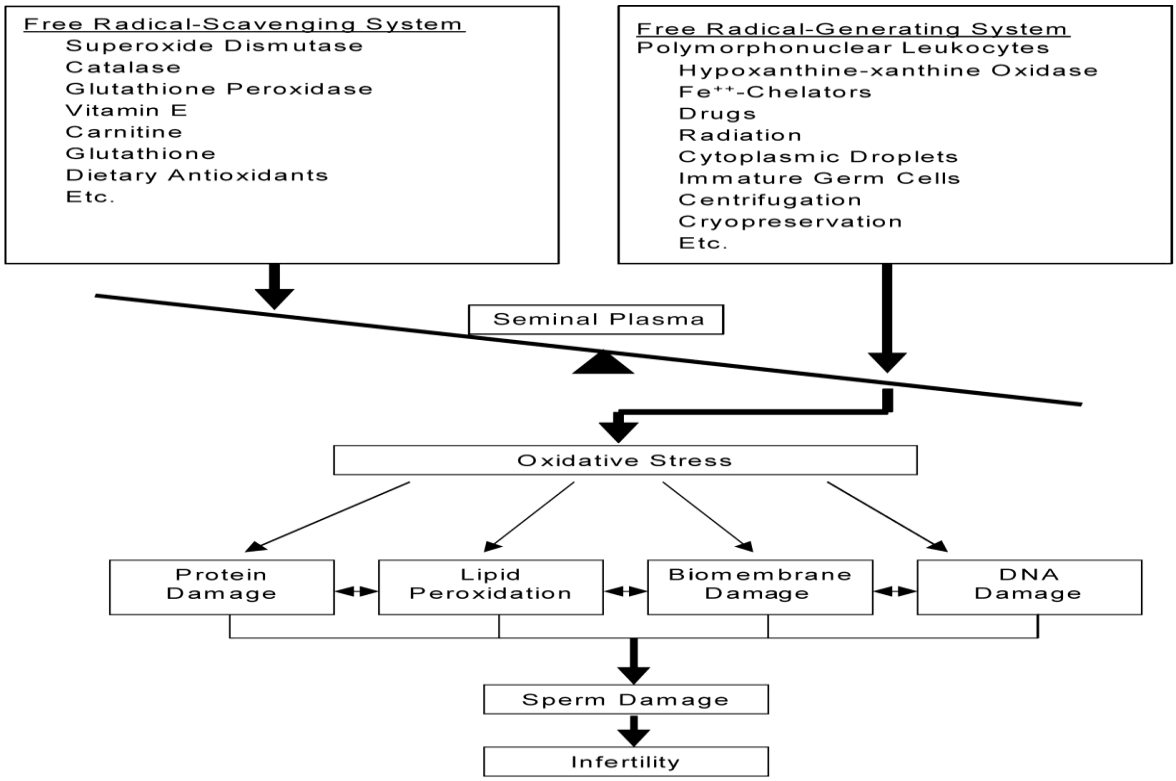

Fig (1): Role of oxidative stress in human body (27).

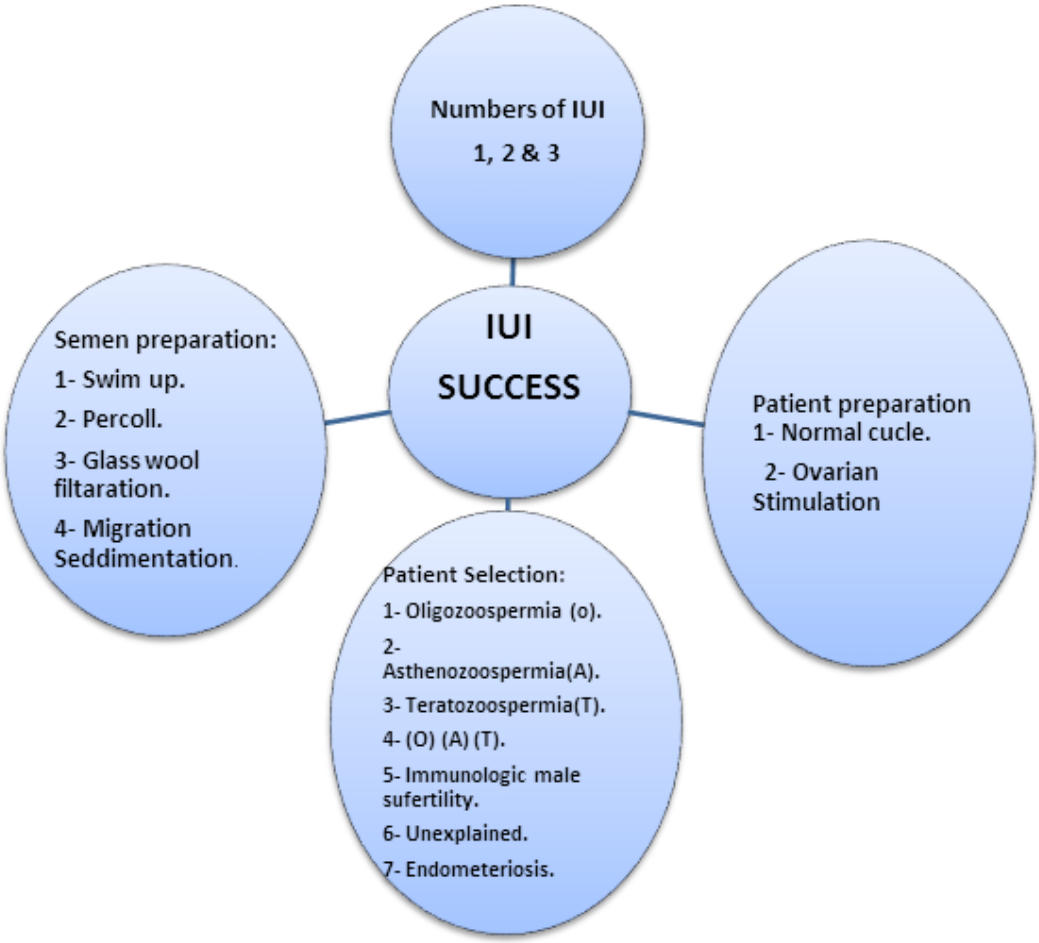

Fig (2): Diagram explain different variables factors control success rates in IUI programmers'.

Material and method:

1. Blood serum was taken from arm blood vessel of women (60 which have positive for CMV and 30 with negative results as control cases) by disposable 5mm syringe.
2. Five milliliters of blood serum was taken from arm blood vessel of women by disposable 5mm syringe.
3. By using Lab. Centrifuge we separate the serum.
4. Kit stripe (CMV IgG and IgM) were used to determined positive and negative results.
5. Enzyme-linked immunoassays also used for titer levels of anti-CMV IgG and IgM.
6. By utilizing Oxis International, Inc. (Foster City, CA, USA) supplied the Bioxytech MDA-586 spectrophotometric assay for MDA assay kit (Catalog No: 21044). Malondialdehyde was measured using an analysis carried out in accordance with the comprehensive instructions included in the kit.
7. IUI done by simple layer and centrifuged method. After 20-30 minute the supernatant which contain the active sperm ant the solution of activation buffer by a syringe.
8. Link the syringes (which contain the sample of husbands) to a special IUI catheter.
9. By Gynecologist the sample housed in to the wife uterus.
10. After one hour the wife can go home.
11. Pregnancy test done after 10 days to IUI.

Statistical analysis: The experiment's results were analyzed using the SPSS Vr.24 software and the t-test with Mont Carlo test (MCP) at the 5% and 1% levels of significance.

Results:

1. Of 60 wives the ages are as following table (1) which explain the role of age in succefull the IUI percent. There are adverse effect of age on this technique;

Table (1): Numbers of wives and ages as a type of parameter.

Numbers	Age	Percent of IUI succeded	P Value	Significance
G1:15	20 – 25	24	G1 and G2 P< 0.01	Yes
G2:20	26- 30	16	G1 and G2 P< 0.01	Yes
G3: 25	31 – 35	14		

Table 2. indicate the results of our study, the number of wives that have positive and negative IgG or/and IgM of CMV disease.

Numbers of wives	IgG	IgM
20	Positive	Negative
4	Negative	Positive
2	Positive	Positive
24	Negative	Negative

2. Comparing the existence of IgG + IgG- and IgM+ or IgM+ for CMV disease, there are a statistically significant difference in the wives who succeed by IUI technique.. Table (3).

Table (3): Show numbers of first IUI succeed and presence of CMV.

No. of IUI succeeded	CMV. IgG positive	CMV. IgG negative	CMV. IgM positive	CMV. IgM negative	P value
8 (50)	2 / 50 (1 %)	4 / 50 (2.5 %)			P < 0.05
4 (50)			1 / 50 (0.5 %)	3/ 50 (1.5)	P < 0.01
1 (50)	+		+		P < 0.05

3. The findings show that the levels of MDA in the serum of women with CMV disease and control groups who underwent IUI procedures differs substantially statistically significantly. Table (4).

Table (4): concentration of MDA in serum of wives infected with Toxoplasmosis disease and control groups that enrolled IUI procedure.

Age	Patients MDA $\mu M\ mL^{-1}$	Controls MDA $\mu M\ mL^{-1}$	P Value	Significance
20 - 25	335±38.16	295.66±40.32	< 0.01	H. Significant
26- 30	342±43.52	312±42.23	< 0.001	H. Significant
31 - 35	351±44.78	321±45.43	< 0.001	H. Significant

According to the findings, there is a statistically significant difference between wives who succeed with IUI and those who do not (P <0.05) when comparing the existence of IgG positive and negative results for CMV infection. Fig.(3).

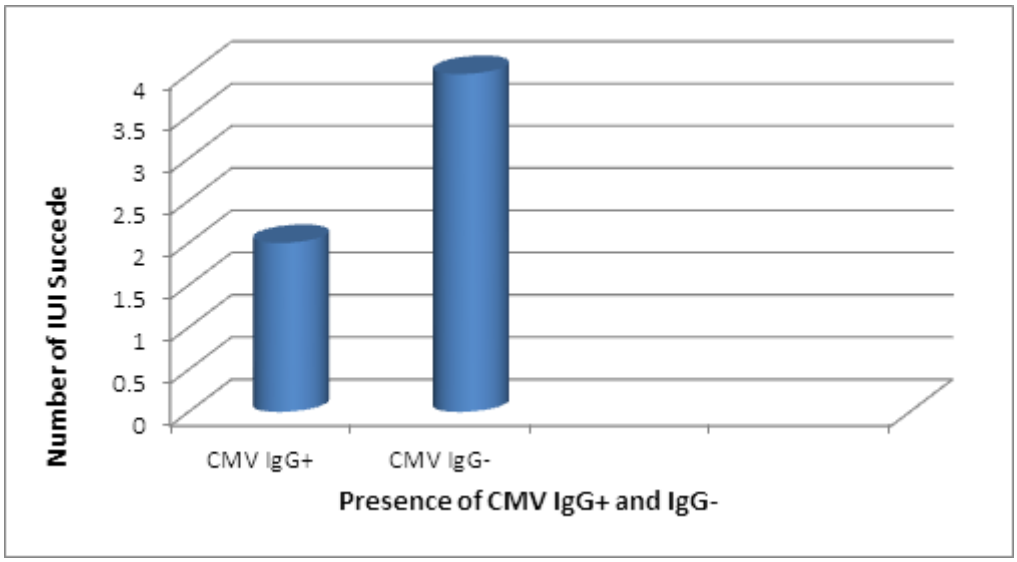

Fig (3): compare between IUI succefull with IgG positive or negative.

4. The data reveal a statistically significant difference between wives who achieve success through IUI procedures and those who do not, with regard to the existence of IgM positive or negative results for CMV disease. (P <0.01) Fig.(4).

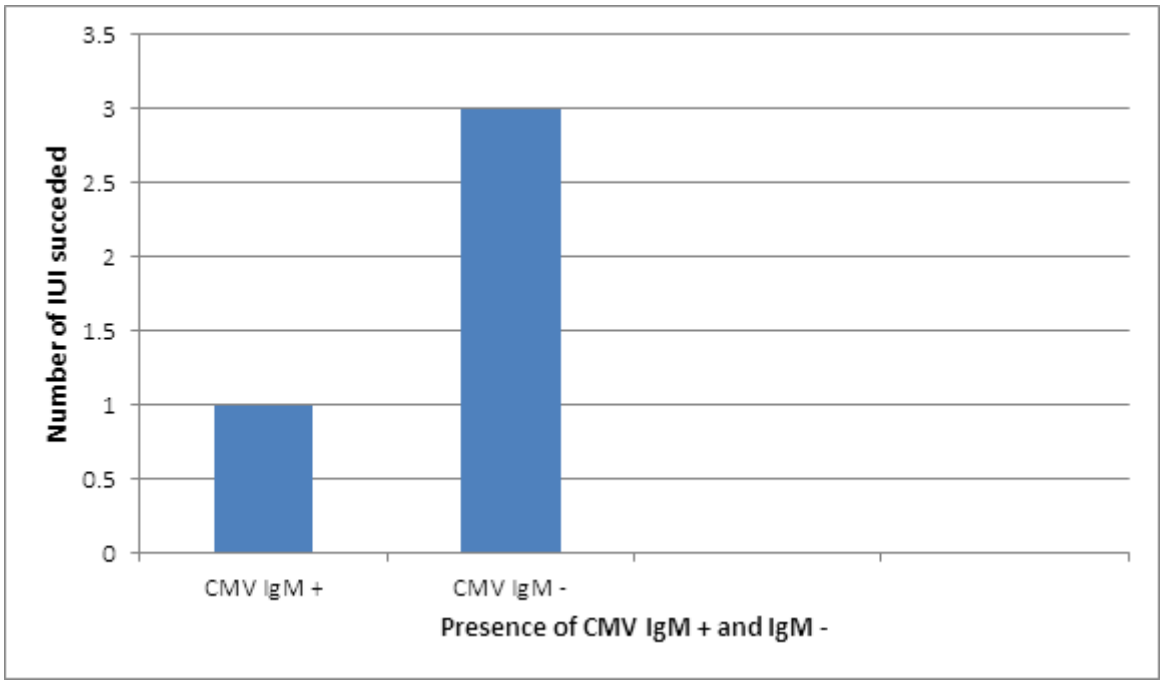

Fig (4): comparison between IUI succefull with IgM- or IgM+.

5. The results find that there are a statistically significant difference in wives that succeed by IUI procedure that not have CMV disease in comparison to infected cases (P <0.05) Table (3).
6. Through the results obtained from the experiment, we found that people with CMV disease have a high oxidative stress than cases which had not positive results with the mentioned disease (P< 0.01). Figure (5).

Discussion:

The variations in sample collection, study design, and geographic location could be the cause of the variations in HCMV prevalent infections throughout the various studies. Each study includes a potential role for the age distribution of infection in women. Jerman et al. (28) studied in (2008-2014), who revealed that American women between the ages of 20 and 24 have the highest rate of spontaneous abortions, while women over 30 have the lowest rate of miscarriages. According to Cannon (1), seroprevalence rises with age when HCMV is acquired in a community and is strongly correlated with both race and socioeconomic position. The kind of HCMV infection is another risk factor; acute infections have a higher mortality rate and are more frequently transmitted to the fetus than recurrent infections (29).

A woman's first pregnancy is a significant moment in her life, and having an abortion is one of her biggest concerns, which has a negative psychological effect on her (29). Infection with cytomegalovirus may occurs at the all ages of peoples, and in United states will infected by this virus within age five years (30). In Europe and North America, the prevalence of HCMV is 80%, but it is around 100% in Africa and Asia (1). Germany had a 56.7% infection incidence, with women having a higher seroprevalence (62.3%) than men (51.0%) (31). Many countries have an endemic human cytomegalovirus (HCMV), and seropositivity rates range from 30% to 100% depending on the location (32). Healthy children and adults do not receive a diagnosis for human cytomegalovirus infection (33). Zhang et al. (34) demonstrated that adult HCMV seropositivity ranges from 55% in industrialized to over 90% in poor nations. Increasing gamete density at the fertilization location is the justification for using artificial insemination. Success rates following IUI treatment processes can vary depending on a number of factors. Methodological changes won't ever be able to address some issues, like the age of the female or the length of her

infertility, for example. On the other hand, a number of variables can be enhanced by employing various tactics (35). When present in cells at low concentrations, free radicals, such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), are essential for a number of physiological processes, including cell differentiation, apoptosis, and vascular tension. On the other hand, too many free radicals can be detrimental, leading to lipid peroxidation, protein deterioration, DNA damage, and aberrant cell death. Certain viral infections cause cells to overproduce free radicals, which aid the virus's replication in a number of ways (36).

Our research indicated that measurement of free radicals as a strong biomarkers can help in minimize the negative effect of this substance on the endometrial secretions and could receptivity of uterus before transfer of the embryo. Several studies (5, 6), showed that positive outcomes from IVF and IUI treatments were associated with reduced levels of oxidative stress, such as catecholamines and lipid peroxidation, and increased levels of antioxidants, such as superoxide dismutases and thioredoxin systems.

Conclusion

Results arise from our study is that there are high positive cases of IgG antibodies for CMV among females in Baghdad population. So that, health education programs that may help in decreasing exposure and contamination primary of this harmful parasite. Also, the prevalence of this disease in subfertil females had a significant higher in comparison to the controls cases, especially in older ages. Besides we suggest that percentage of prosperity rate of IUI and IVF may increased by lowering the percent of infectin. It is important to suggestion more and further studies to explain the mechanisms by which this disease do its unwanted problems.

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