

The Possible Etiological Role of CMV & EBV Latent Infections in Polycystic Ovary Syndrome Iraqi patients

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ABSTRACT

To investigate whether or not there is a causal relationship between latent infection of CMV & EBV and polycystic ovary syndrome (PCOS) in a sample of Iraqi women, 60 blood samples were obtained from PCOS patients with age range (20-40) years who attended Kamal Al-Samaria IVF Center in Baghdad-Iraq, and (30) blood samples from apparently healthy age-matched women. By using ELISA technique anti-CMV & anti-EBV IgG specific Abs were explored in sera separated from blood samples of both patients and controls. The results revealed that 10 (≈16.7%) out of the 60 PCOS women were positive for CMV compared to only one (≈3.3%) positive case recorded in the control group. On the other hand, positive results of anti-EBV IgG Abs were recorded in 27 (≈45%) out of the 60 cases of women with PCOS, in comparison, no one (0%) of the 30 control women was positive for this test. Such results provide objective indications for these viruses as being involved in an aspect of causal events behind PCOS.

Keywords: PCOs, EBV, CMV, Fertility

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Introduction

Polycystic ovary syndrome is a heterogeneous disorder with many pathophysiological proprieties which include ovulatory dysfunction, increased androgen production, disordered gonadotropin secretion, and polycystic ovarian morphology (PCOM). It also has many neuroendocrine features including increased serum concentration of luteinizing hormone (LH), increased LH/FSH ratio, and increase in amplitude and frequency of pulsatile LH secretion [1-3]. Polycystic ovary syndrome leads to many complications such as oligomenorrhea, anovulation, and infertility [4]. It has been recorded to be of high prevalence (20-33%) in different societies [5]. Worldwidely there were 116 million women afflicted with PCOS [6]. Evidence indicates that PCOS is a pro-inflammatory disorder, furthermore, studies raise the possibility of an intriguing association of PCOS with low-grade infections [7].

Epstein-Barr virus (EBV) as one of the known human herpesvirus types in the herpes virus family spread most commonly through bodily fluid primarily saliva. It infects more than 90% of the world population. EBV predominantly infects resting B-lymphocyte through the complement receptor (CD21), the only known B cell receptor for EBV [8]. Even though the infection is usually self-limited, and the virus persists latently in the host within long-life memory B cells [9]. Cytomegalovirus (CMV) is a prevalent viral pathogen in the family herpesviridae. Humans and monkeys serve as a natural host. Despite of the cellular immune response evolved by the host against CMV [10], however, the virus avoids the immune attack and stay hidden inside host cells, as a result, CMV is never eliminated totally from infected individuals, causing persistent asymptomatic infection. Following the subclinical primary CMV infection, the virus and the immune system can reach a homeostatic balance. Denotations have indicated that CMV may contribute to the development of many diseases including vascular diseases and atherosclerosis and have also outlined the

deleterious effect on immune senescence, beside its effects on general health outcomes [11].

Acquiring an infection with CMV in utero or immediately after birth causes clinical complications as a consequence of the incapability of the immature host to eliminate the primary infection converting the virus into latency. EBV can inhibit immunity by inducing infected B lymphocyte to produce IL-10 that inhibits the activity of antigen presenting cells, while the inhibitory mechanism of CMV depends on the inhibition of antigen presentation via inhibition of the proteasomal activity [12-14].

The goal of this study is to disclose the probable causal relationship between latent CMV & EBV infections with PCOS in Iraqi Females.

Materials and Methods

This study was carried out in Kamal Al-Samarrai infertility treatment and in vitro fertilization hospital, in which a total number of 90 women with age range 20-40 years were enrolled voluntarily. They have included 60 females who were diagnosed to be PCOS patients in addition to 30 apparently healthy women. The diagnosis of PCOS was based on Rotterdam 2003 criteria by two of three following features (Rotterdam ESHRE/ASRM consensus, 2004), Oligoovulation and/or non-ovulation, and biochemical signs and/or clinical signs of hyperandrogenism (such as hirsutism, alopecia and acne). The appearance of polycystic ovaries on ultrasound (Morphological changes of the ovaries were diagnosed using transvaginal ultrasound). The control group was submitted to ultrasound examination and has normal hormonal status with regular menstrual cycles. Peripheral blood was withdrawn from each participant by the usual venipuncture procedure. Sera were separated and kept frozen (-20) until use. ELISA technique was performed to detect anti-CMV and anti-EBV IgG antibodies in patients and controls using commercially available kits (Human cytomegalovirus IgG; bioactive diagnostic and Human EBV VCA IgG; IMMUNOLAB GmbH).

Results and Discussion

This study aimed to trace CMV & EBV latent Infections by detecting specific IgG Abs in sera of PCOS patients in comparison with healthy controls. The whole results are summarized in the table -1-and table -2-which demonstrate positive cases for CMV and EBV and the percentage distribution for both viruses. It has been recorded that 10 out of the 60 cases of PCOS patients, with a percentage of approximately 16.66%, were CMV positive compared to only one case (3.33%) recorded positive results among the 30 apparently healthy women.

Table 1. Prevalence of anti-CMV Abs in patients with PCOS and controls.

Groups	CMV IgG	
	Serum	Distribution of CMV (%)
Healthy (Control) (No.=30)	(1) +ve, (29) -ve	3.33
Patients (No.=60)	(10) +ve, (50) -ve	16.66

(P=0.069)

Table 2. Prevalence of anti-EBV Abs in patients with PCOS and controls.

Groups	EBV IgG	
	Serum	Distribution of EBV (%)
Healthy (Control) (No.=30)	(0) +ve, (30) -ve	0.00
Patients (No.=60)	(27) +ve, (33) -ve	45.00

(P=0.000)

On the other hand, anti-EBV IgG antibody recorded to be positive in 27 out of the 60 patients with a percentage of approximately 45% in comparison, no one (0%) of the control group member's revealed a positive result. Statistically, the difference was of significant importance (P = 0.000).

One can be deduced that what accompanying these infections of chronic low-grade inflammatory events can stand behind some of the underlying causes of PCOS. There were few other studies have dealt with the same topic, one of which was a study accused some other pathogens and by using a microimmunofluorescence test it detected anti-Chlamydia pneumonia and anti-Chlamydia trachomatis specific IgG Abs in PCOS patients.

The study suggested that chronic inflammation accompany chlamydial infection could contribute to the pathogenic process that leads to the metabolic and hormonal disorders of PCOS [15].

In the same context different relevant studies referred to the inflammatory bases of PCOS [16, 17]. Some other studies directed attention to *Helicobacter pylori*, as the researchers found significantly higher seropositivity in PCOS patients in comparison to that in controls [18, 19].

Conclusion

Chronic low-grade Inflammation which associates CMV and EBV may contribute one way or another in hormonal and metabolic disorders, involving the hypothalamic

pituitary adrenal (HPA) axis our central stress response system, that contributes to the emergence of PCOS.

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